Decision Memo for Surgery for Diabetes (CAG-00397N)

Decision Summary

The Centers for Medicare & Medicaid Services (CMS) has determined the following:

1) The evidence is not adequate to conclude that open and laparoscopic Roux-en-Y gastric bypass (RYGBP), laparoscopic adjustable gastric banding (LAGB), and open and laparoscopic biliopancreatic diversion with duodenal switch (BPD/DS) improve health outcomes in Medicare beneficiaries who have type 2 diabetes mellitus (T2DM) and a body-mass index (BMI) < 35. Therefore, these procedures are not reasonable and necessary for patients with type 2 diabetes and BMI < 35 under section 1862(a)(1)(A) of the Social Security Act.

2) The evidence is adequate to conclude that open and laparoscopic Roux-en-Y gastric bypass (RYGBP), laparoscopic adjustable gastric banding (LAGB), and open and laparoscopic biliopancreatic diversion with duodenal switch (BPD/DS) improve health outcomes in Medicare beneficiaries who have T2DM and a BMI $\geq$ 35. Type 2 diabetes mellitus is a comorbid condition related to obesity as defined in NCD Manual 100.1 (Bariatric Surgery for Treatment of Morbid Obesity).

This decision makes no changes to National Coverage Determination (NCD) Manual section 100.8 (Intestinal Bypass Surgery) and section 100.11 (Gastric Balloon for Treatment of Obesity). Treatments for obesity alone remain non-covered.

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Decision Memo

TO: Administrative File: CAG-00397N
Surgery for Diabetes

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SUBJECT: Coverage Decision Memorandum for Surgery for Diabetes
DATE: February 12, 2009

I. Decision

The Centers for Medicare & Medicaid Services (CMS) has determined the following:

1) The evidence is not adequate to conclude that open and laparoscopic Roux-en-Y gastric bypass (RYGBP), laparoscopic adjustable gastric banding (LAGB), and open and laparoscopic biliopancreatic diversion with duodenal switch (BPD/DS) improve health outcomes in Medicare beneficiaries who have type 2 diabetes mellitus (T2DM) and a body-mass index (BMI) < 35. Therefore, these procedures are not reasonable and necessary for patients with type 2 diabetes and BMI < 35 under section 1862(a)(1)(A) of the Social Security Act.

2) The evidence is adequate to conclude that open and laparoscopic Roux-en-Y gastric bypass (RYGBP), laparoscopic adjustable gastric banding (LAGB), and open and laparoscopic biliopancreatic diversion with duodenal switch (BPD/DS) improve health outcomes in Medicare beneficiaries who have T2DM and a BMI $\geq$ 35. Type 2 diabetes mellitus is a comorbid condition related to obesity as defined in NCD Manual 100.1 (Bariatric Surgery for Treatment of Morbid Obesity).

This decision makes no changes to National Coverage Determination (NCD) Manual section 100.8 (Intestinal Bypass Surgery) and section 100.11 (Gastric Balloon for Treatment of Obesity). Treatments for obesity alone remain non-covered.

II. Background

Diabetes is a disease in which insulin is absent or not functionally available in sufficient quantities to metabolic pathways including those for glucose utilization. Historically, diabetes has been broadly classified as type 1 diabetes mellitus (T1DM; formerly called type I, insulin-dependent diabetes mellitus (IDDM) or juvenile diabetes) and type 2 diabetes mellitus (T2DM; formerly called type II, non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes) with the distinguishing features largely based on clinical presentation. T1DM is generally associated with an earlier age of onset, thinner patients and ketosis, whereas T2DM is associated with a later age of onset and weight gain. T1DM accounts for 5 to 10% of diabetic patients and results from immune-mediated destruction of the pancreatic islet cells including pancreatic beta cells. T2DM accounts for 90 to 95% of diabetic patients and is generally characterized by insulin resistance.

Epidemiology

Overall, the prevalence of diabetes in the United States is 7.9 %; 6.8% in men and 8.9% in women. The prevalence of diabetes increases with increasing age; approximately 11-15% over age 50 as compared to 6.6% or less in lower age groups. It is highest in blacks (11.2%) and lowest in whites (7.2%). Data from the Behavioral Risk Factor Surveillance System (BRFSS) in 2001 show that obesity is significantly associated with a higher rate of diabetes. Compared with adults with normal weight, adults with a BMI of 35-39.9 are 3.44 times more likely to have diabetes and adults with a BMI of 40 or higher are 7.37 times more likely of having diagnosed diabetes. The prevalence of diabetes in persons with BMIs from 35 to 39.9 is 14.9% and 25.6% in persons with BMIs $\geq$ 40.

Diabetes mellitus is commonly managed with dietary modification and medications. With the exception of pancreatic transplant, there are no common surgical procedures that are intended to treat diabetes. In addition, Medicare will pay for the routine costs, as well as transplantation and appropriate related items and services, for Medicare beneficiaries participating in a National Institutes of Health (NIH)-sponsored clinical trial of islet cells transplantation (NCD 260.3.1). However, surgical procedures used for weight loss in morbidly obese persons have been noted to reduce medication use and in some cases eliminate diabetes altogether. The same procedures have been proposed to treat diabetes mellitus in persons who are not morbidly obese.

Several modifications of bariatric surgery have developed over the last several years. Two major types of surgery are now being employed. One type diverts food from the stomach to a lower part of the digestive tract where the normal mixing of digestive fluids and adsorption of nutrients cannot occur – a malabsorptive procedure. The other type restricts the size of the stomach and decreases intake – a restrictive procedure. Other surgeries combine both types of procedures. Initially, bariatric surgery was developed as an open procedure, but in recent years, successful attempts have been made to convert some of the procedures to laparoscopic procedures, while new ones have been developed solely as laparoscopic procedures. The following are descriptions of bariatric surgery procedures:

Roux-en-Y Gastric Bypass (RYGBP) (Open/Lap)
RYGBP achieves weight loss through both gastric restriction and malabsorption. Reduction of the stomach to a small gastric pouch (30 cc) results in feelings of satiety following even small meals. This small pouch is connected to a segment of the jejunum, bypassing the duodenum and very proximal small intestine, thereby reducing absorption. The RYGBP procedure has been performed regularly since the early 1980s and was first performed laparoscopically in the early 1990s. RYGBP is one of the most common types of weight loss procedures in current use, with approximately 50,000 cases performed in 2001.

Biliopancreatic Diversion (BPD) with and without Duodenal Switch (DS) (Open/Lap)
BPD/DS, like RYGBP, combines both restrictive and malabsorptive mechanisms. The stomach is partially resected, but the remaining capacity is generous compared to that achieved with the RYGBP. As such, patients eat relatively normal-sized meals and do not need to restrict intake radically, since the most proximal areas of the small intestine (i.e., the duodenum and jejunum) are bypassed, and substantial malabsorption occurs. Although this procedure is less commonly performed than either banding procedures or RYGBP, the approach is strongly favored by some bariatric surgeons because this procedure appears to yield higher Excess Weight Loss (EWL). The partial biliopancreatic diversion with duodenal switch is a variant of the BPD procedure. Recently, a number of centers in the United States and Canada have begun to perform this procedure, which involves resection of the greater curvature of the stomach, preservation of the pyloric sphincter, and transection of the duodenum above the ampulla of Vater with a duodeno-ileal anastamosis and a lower ileo-ileal anastamosis.

Laparoscopic Adjustable Gastric Banding (LABG) (Lap)

Gastric banding achieves weight loss by gastric restriction, not malabsorption. A band creating a gastric pouch with a capacity of approximately 15 to 30 cc encircles the uppermost portion of the stomach. The band is an inflatable doughnut-shaped balloon, the diameter of which can be adjusted in the clinic by adding or removing saline via a port that is positioned beneath the skin. The bands used today are adjustable, allowing the size of the gastric outlet to be modified as needed, depending on the rate of a patient's weight loss. Today, essentially all of the banding procedures are performed laparoscopically. The open version of adjustable gastric banding (AGB) is not performed at present.

Sleeve Gastrectomy (Open/Lap)
Sleeve gastrectomy is a 70%-80% greater curvature gastrectomy (sleeve resection of the stomach) with continuity of the gastric lesser curve being maintained while simultaneously reducing stomach volume. It may be the first step in a two-stage procedure when performing RYGBP.

Vertical Gastric Banding (VBG) (Lap)
VBG uses mechanical restriction to cause weight loss, a similar mechanism to that used in LAGB, with no malabsorption component. However, the upper part of the stomach is stapled, creating a narrow gastric inlet or pouch that remains connected with the remainder of the stomach. In addition, a non-adjustable band is placed around this new inlet in an attempt to prevent future enlargement of the stoma (opening). As a result, patients experience a sense of fullness after eating small meals. Weight loss from this procedure results entirely from eating less. VBG was one of the more common surgical procedures for weight loss in the late 1980s and early 1990s but has been largely supplanted by LAGB since 1995. Now its role in the treatment of patients with severe obesity is limited. VBG is essentially no longer performed.

On May 19, 2008, CMS initiated a national coverage analysis regarding the use of gastric bypass and other types of surgery for treatment of diabetes. Our goal is to assess the evidence for the ability of various gastric and intestinal bariatric surgery procedures to improve diabetes status among obese, overweight, and non-overweight diabetics. We are not reconsidering current coverage determinations for types of surgery for morbid obesity in the NCD Manual section 100.8 (Intestinal Bypass Surgery) and section 100.11 (Gastric Balloon for Treatment of Obesity).

III. History of Medicare Coverage

Current Coverage Policies

NCD Manual Section 40.5 *Obesity*
Obesity may be caused by medical conditions such as hypothyroidism, Cushing's disease, and hypothalamic lesions, or can aggravate a number of cardiac and respiratory diseases as well as diabetes and hypertension. Services in connection with the treatment of obesity are covered when such services are an integral and necessary part of a course of treatment for one of thesemedical conditions. However, program payment may not be made for treatment of obesity unrelated to such a medical condition since treatment in this context has not been determined to be reasonable and necessary.

NCD Manual Section 100.1 *Bariatric Surgery for Morbid Obesity*
This NCD covers open and laparoscopic Roux-en-Y gastric bypass (RYGBP), laparoscopic adjustable gastric banding (LAGB), and open and laparoscopic biliopancreatic diversion with duodenal switch (BPD/DS), are reasonable and necessary for Medicare beneficiaries who have a body-mass index (BMI) $\geq$ 35, have at least one co-morbidity related to obesity, and have been previously unsuccessful with medical treatment for obesity. Procedures must be performed at facilities that are: (1) certified by the American College of Surgeons (ACS) as a Level 1 Bariatric Surgery Center (program standards and requirements in effect on February 15, 2006); or (2) certified by the American Society for Bariatric Surgery as a Bariatric Surgery Center of Excellence (BSCOE) (program standards and requirements in effect on February 15, 2006).

NCD Manual Section 100.8 *Intestinal Bypass*
This NCD noncovers intestinal bypass surgery for treatment of obesity**.**

NCD Manual Section 100.11 *Gastric Balloon*
This NCD noncovers gastric balloon procedure for treatment of obesity.

Benefit Category Determination

Under §1861(q) of the Social Security Act (the Act) bariatric surgery is a physician service, and as such qualifies as a benefit. Evaluation and management services of patients with obesity for whom bariatric surgical procedures are contemplated may also be considered to be a benefit as physicians' services.

Bariatric surgery procedures may be considered to be a benefit as inpatient hospital services under §1861(b) of the Act and certain services and supplies may be considered to be a benefit to hospital outpatients under §18619(s)(2)(B) of the Act, “incident to” a physician’s service.

IV. Timeline of Recent Activities

5/19/2008	CMS initiates opening a NCD for surgery for diabetes. Initial 30-day public comment period begins
6/18/2008	Initial 30 day public comment period closes. Comments posted on the website.
11/17/2008	Proposed Decision Memorandum is posted and 30-day public comment period begins.

V. FDA Status

Surgical procedures are not subject to FDA approval. However, LapBands™ are utilized in some bariatric surgery and the date and content of FDA approval for this device can be found at http://www.fda.gov/cdrh/mda/docs/p000008.pdf.

VI. General Methodological Principles

When making national coverage determinations under §1862(a)(1)(A) of the Social Security Act, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A. In general, features of clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, and the blinding of readers of the index test, and reference test results.

Public comment sometimes cites the published clinical evidence and gives CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction

We searched Medline for articles on bariatric surgery and its effects on improvement or resolution of diabetes for all BMI ranges to see if resolution/improvement of diabetes was related to and/or independent of BMI level. We utilized selected articles and we utilized selected references from articles we found were relevant to evaluate this question.

The acceptable studies concentrated on the outcome of improvement or resolution of abnormal blood glucose measures in persons diagnosed with diabetes who had or did not have bariatric surgery. Since our current coverage decision allows the use of bariatric surgery in diabetic patients with a BMI $\geq$ 35, we have divided the discussion of evidence reviewed according to BMI using a cut-point of 35. We did not include articles that used resolution of metabolic syndrome (which can include diabetes) as the only outcome for two reasons. Metabolic syndrome is commonly defined as having three or more of a set of five abnormalities (waist circumference $\geq$102 cm in men and 88 cm in women; serum triglyceride level of $\geq$150 mg/dL; high-density lipoprotein cholesterol (HDL-C) level of $\leq$ 40 mg/dL in men and 50 mg/dL in women; blood pressure $\geq$130/85 mm Hg; and serum glucose $\geq$110 mg/dL). Therefore, a patient with metabolic syndrome may or may not have diabetes and a patient whose diabetes resolved might still have metabolic syndrome. Furthermore, there is not a standardized definition for metabolic syndrome and some papers did not provide a definition.

B. Discussion of Evidence

1. Question

For this NCD, the question of interest is:
Is the evidence sufficient to conclude that the following bariatric surgery procedures will improve health outcomes for Medicare patients with diabetes:

a. Roux-en-Y gastric bypass;
b. Laparoscopic adjustable gastric banding;
c. Biliopancreatic diversion with duodenal switch; or
d. Sleeve gastrectomy?

2. External technology assessment (TA)

None were identified and CMS did not commission a TA for this NCA.

3. Internal technology assessment

Evidence

BMI ≥ 35

Long-Term Mortality after Gastric Bypass Surgery. Adams 2007.
Age ≥ 65: None, mean age 39
N= 9949
M:F: 1592:8357
BMI: 44.9 ± 7.6
Surgical type: RYGBP
Retrospective cohort study

The Adams et al. NEJM article (2007) reported a retrospective cohort study of long-term mortality (from 1984 to 2002) among 9949 patients who had undergone gastric bypass surgery and 9628 severely obese persons who applied for driver's licenses. From these subjects, 7925 surgical patients and 7925 severely obese control subjects were matched for age, sex, and body-mass index. The National Death Index was used to determine the rates of death from any cause and from specific causes. Data on the estimated weight loss (EWL) were not available. During a mean follow-up of 7.1 years, adjusted long-term mortality from any cause in the surgery group decreased by 40%, as compared with that in the control group (37.6 vs. 57.1 deaths per 10,000 person-years, p< 0.001) while mortality from diabetes in the surgery group decreased by 92% (0.4 vs. 3.4 per 10,000 person-years, P = 0.005). Among other conclusions by the authors, long-term total mortality after gastric bypass surgery was significantly reduced, particularly deaths from diabetes.

Resolution of diabetes mellitus and metabolic syndrome following Roux-en-Y gastric bypass and a variant of biliopancreatic diversion in patients with morbid obesity. Alexandrides 2007.
Age ≥ 65: None
N= 137
M:F: 31:106
BMI: 46.1± 2.9 RYGBP, 59.7± 10.6 BPD
Surgical type: RYGBP, BPD-RYGBP variant
Retrospective cohort study

The objective of this study by Alexandrides et al. (2007) was to investigate the effects of RYGBP and BPD-RYGBP, a variant of BPD which has a lower rate of metabolic deficiencies than BPD, on T2DM and the major components of metabolic syndrome in patients with morbid obesity and T2DM. Their prospective database from June 1994 until May 2006 was analyzed and 137 patients with TDM2 (of 745 total patients) were found. Twenty six of these underwent RYGBP (BMI 46.1 ± 2.9 kg/m^2) and 111 BPD-RYGBP (BMI 59.7 ± 10.6 kg/m^2). Seven of the patients were on insulin (4.90%) and 37 on oral hypoglycemic agents (25.87%). Pre- and postoperative medications and clinical and biochemical parameters were considered in the analysis. The mean follow-up was 26.39 ± 21.17 months. EWL averaged 70% after either procedure.

T2DM resolved in 89% and 99% of the cases following RYGBP and BPD-RYGBP, respectively. Two years after BPD-RYGBP all the patients had blood glucose < 110 mg/dl, 95% had normal cholesterol, 92% normal triglycerides and 82% normal blood pressure. The respective values following RYGBP were 66%, 33%, 78% and 44%. Uric acid decreased significantly only after BPD-RYGBP. Liver enzymes improved in both groups. Mortality was 0% in the 26-patient group and 1 of 111 in the other group (0.9%)

The authors concluded that RYGBP and BPD-RYGBP were safe and lead to normalization of blood glucose, lipids, uric acid, liver enzymes and arterial pressure in the majority of patients, although this variant of BPD was more effective than RYGBP alone. They suggested that further studies should also investigate its usefulness in patients with milder degrees of obesity, DM2 and metabolic syndrome.

Bariatric Surgery A Systematic Review and Meta-analysis. Buchwald 2004 JAMA.

Age ≥ 65: None
N= 22094
M:F: 19:73 (not reported for 1573 (8%) patients)
BMI: Mean 46.9, Range 32-68
Surgical Type: Mostly GBP, Banding Bariatric Surgery, Gastroplasty, BPD
Meta-analysis

Buchwald's meta-analysis (2004) had as its objective determining the impact of bariatric surgery on weight loss, operative mortality outcome, and four obesity comorbidities (diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea). First, the authors utilized an electronic literature search of MEDLINE, Current Contents, and the Cochrane Library databases plus manual reference checks of all articles on bariatric surgery published in the English language between 1990 and 2003. Two levels of screening were then used on 2738 citations. A total of 134 fully extracted studies, which included 91 overlapping patient populations (kin studies), were included. The 134 studies included 179 treatment groups and 22094 patients either enrolled or analyzable in the data set, including those in comparator control groups. Included were five randomized controlled trials, 28 nonrandomized controlled trials or series with comparison groups, and 101 uncontrolled case series. At least 1 categorical outcome of interest (e.g., proportion of patients with resolution or improvement in diabetes, hyperlipidemia, hypertension, or obstructive sleep apnea) or one continuous outcome of interest (change in a laboratory or physiological measure) was reported by each of the extracted studies. For the calculation of the percentage resolved, for a particular comorbidity, the authors included those studies reporting the number of patients in which comorbid conditions disappeared or no longer required therapy. Nineteen percent of the patients were men and 72.6% were women, with a mean age of 39 years (range, 16-64 years). Sex was not reported for 1537 patients (8%). The baseline mean body mass index for 16,944 patients was 46.9 (range, 32.3-68.8).

Within studies reporting resolution of diabetes, 1417 (76.8% [meta-analytic mean, 76.8%; 95% CI, 70.7%-82.9%]) of 1846 patients experienced complete resolution. Within studies reporting both resolution and improvement or only improvement of diabetes, 414 (85.4% [meta-analytic mean, 86.0%; 95% CI, 78.4%-93.7%]) of 485 patients experienced resolution or improvement of diabetes. By type of bariatric surgical procedure and with respect to diabetes resolution, there was a gradation of resolution effect from 98.9% (95% CI, 96.8%-100%) for biliopancreatic diversion or duodenal switch, to 83.7% (95% CI, 77.3%-90.1%) for gastric bypass, to 71.6% (95% CI, 55.1%-88.2%) for gastroplasty, and to 47.9% (95% CI, 29.1%- 66.7%) for gastric banding.

In patients selected for diabetes or impaired glucose tolerance at baseline, the mean change in percentage of excess weight loss was 57.25% (95% CI, 46.21%-68.30%) and the reduction in BMI was 14.03 (95% CI, 10.77- 17.30), both of which are close to the values found for unselected bariatric surgical populations.

The reduction in fasting glucose levels was significantly different for the total diabetic population (mean change, 71.53 mg/dL; 95% CI, 49.37-93.69 mg/dL, n= 296 by meta-analysis) compared with unselected bariatric surgical populations (mean change, 13.33 mg/ dL; 95% CI, 10.81-15.86 mg/dL, n= 2092 by meta-analysis).

Using a random effects model in the meta-analysis the mean (95% confidence interval) percentage of excess weight loss (EWL) varied from approximately 47% to 70% depending on the type of procedure. Diabetes was completely resolved in 76.8% of patients and resolved or improved in 86.0%. The authors concluded that a substantial majority of patients with diabetes experienced complete resolution or improvement.

Hormonal changes after Roux-en Y gastric bypass for morbid obesity and the control of type-II diabetes mellitus. Clements 2004.
Age ≥ 65: None
N= 25
M:F: 5:20
BMI: 52.7 ± 8.8
Surgical Type: RYGBP
Retrospective cohort study

To test the hypothesis that gastrointestinal hormonal changes explain the resolution of T2DM, Clements (2004) preoperatively evaluated 20 morbidly obese (MO) patients with T2DM and enrolled in this IRB-approved protocol, for demographics and fasting levels of the following: glucose, insulin, C-peptide, glucagon, cortisol, gastric inhibitory polypeptide (GIP), and glucagon-like peptide-1 (GLP-1). Each patient underwent RYGBP with a 15-cc gastric pouch and 150-cm Roux limb. Postoperatively, each of the variables was measured at two weeks, six weeks, and 12 weeks and compared with the preoperative result using a Student t test with significance level of p = 0.05.

There were five male and 15 female patients, average age 40.3 ± 7.9 (SD) years, weight 146.3 ± 34.0 kg, height 158.7 ± 18.7 cm, and BMI 52.7 ± 8.8. Weight and BMI decreased progressively (117.5 ± 26.9 kg and 47.0 ± 7.4, p = 0.01, respectively) during the study but reached significance only at 12 weeks. Fasting plasma glucose decreased significantly within 2 weeks after surgery. Insulin and cortisol both approached, but never achieved, significant changes over 12 weeks. GLP-1 increased initially, but not significantly. GIP and C-peptide both decreased significantly. Glucagon remained essentially unchanged over 12 weeks.

The authors concluded that RYGBP rapidly normalizes fasting plasma glucose in morbidly obese patients with T2DM and that GIP, a factor in the enteroinsulin axis, decreases and may play a role in the correction of T2DM after gastric bypass.

Improvement of Insulin Resistance After Obesity Surgery: A Comparison of Gastric Banding and Bypass Procedures. Lee WJ 2008a.
Age ≥ 65: None
N= 660
M:F: 197:463
BMI: 41.3± 6.7 LVGB, 41.9± 6.9 LAGB
Surgical Type: LVGB 82% and LAGB 18%
Retrospective Cohort Study

The basis of this study by Lee et al. (2008) was to find the true mechanism for improving T2DM after bariatric surgery. This trial assessed the effect of duodenal jejunal exclusion on the resolution of insulin resistance (IR) in gastric banding and gastric bypass procedures. In 660 patients with complete biochemical and clinical data at baseline and at three years, there were 197 males and 463 females. The mean age was 31.5 years (range 18-64) and mean BMI was 41.4 (32-77). Five hundred forty four patients had LGBP and 116 patients had LAGB. IR was measured by homeostatic model assessment (HOMA) index (HI), calculated as HI = plasma glucose (mmol/l) x insulin (UI/ml)/22.5. HI was measured before surgery and one, three, six, 12, 24, and 36 months after surgery. Of the 660 individuals, 517 (78.4%) had IR. The mean HI was 7.62 ± 13.13. The HI was correlated with BMI, waist circumference, insulin resistance, hyperlipidemia, inflammatory indicators, and abnormal liver enzymes. Before surgery, the HI was 7.92 ± 14.18 for the bypass group and 6.27 ± 6.47 for the banding group. After surgery, the HI began to lower in both groups, and this reduction was maintained during follow-up. At 36 months after surgery, mean percentage of excess weight loss (%EWL) was 70.5% for the bypass group and 41.9% for the banding group. The HI was 1.00 ± 0.79 for bypass and 1.51 ± 1.25 for banding. The bypass patients had a better and faster weight reduction, but the HI was similar between the two groups at the same weight reduction percentage. The authors concluded that IR is common in morbidly obese patients. Both gastric banding and gastric bypass are effective for reversing IR in these patients, related to the absolute weight loss rather than the type of surgical procedure. No duodenal-jejunal exclusion effect on IR resolution was observed in this study.

Weight loss in severely obese subjects prevents the progression of impaired glucose tolerance to type II diabetes. A longitudinal interventional study. Long 1994.

Age ≥ 65: None
N= 163
M:F: 23:140
BMI: All >45
Surgical Type: RYGBP
Retrospective observational study

Long et al. (1994) aimed a study at determining if weight loss might prevent conversion of impaired glucose tolerance (IGT) to diabetes. The authors stated that the prevalence of IGT in the U.S. population is estimated at 11.2%, more than twice that of diabetes and that because an oral glucose tolerance test is needed for its detection, most of these patients are undiagnosed. They postulated that screening for IGT would be meaningful if progression to diabetes could be delayed or prevented.

For an average of 5.8 years (range 2-10 years), 136 individuals with IGT and clinically severe obesity (> 45 kg excess body weight) were followed. The experimental group included 109 patients with IGT who underwent bariatric surgery for weight loss. The control group was made up of 27 subjects with IGT who did not have bariatric surgery. The criteria of the World Health Organization were used to detect IGT and diabetes in this population. The main outcome measure of this nonrandomized control trial was the incidence of diabetes divided by the time of exposure to risk.

Of the 27 subjects in the control group, six developed diabetes during an average of 4.8 ± 2.5 years of post-diagnosis follow-up, yielding a rate of conversion to diabetes of 4.72 cases per 100 person-years. The 109 individuals in the experimental group were followed for an average of 6.2 ± 2.5 years post-bariatric surgery. Based on the 95% confidence interval of the comparison group, they expected that between 22 and 36 subjects in the experimental group would develop diabetes over the follow-up period. Only one of the 109 experimental-group patients developed diabetes, resulting in a conversion rate of the experimental group of only 0.15 cases per 100 person-years, significantly lower ($p < 0.0001$) than the control group.

The authors concluded that weight loss in patients with clinically severe obesity prevents the progression of IGT to diabetes by > 30-fold.

The gastric bypass operation reduces the progression and mortality on non-insulin-dependent diabetes mellitus. MacDonald 1997.
Age ≥ 65: None
N= 232
M:F: 63:169
BMI: Mean 50
Surgical Type: RYGBP
Retrospective Cohort study

In a study by MacDonald et al. (1997), 154 of 232 morbidly obese patients with non-insulin-dependent diabetes mellitus referred to East Carolina University between March 5, 1979, and January 1, 1994, had a Roux-en-Y gastric bypass operation and 78 did not undergo surgery because of personal preference or their insurance company's refusal to pay for the procedure. The surgical and the nonoperative (control) groups were comparable in terms of age, weight, body mass index, sex, and percentage with hypertension. The two groups were compared retrospectively to determine differences in survival and the need for medical management of their diabetes. Mean length of follow-up was 9 years in the surgical group and 6.2 years in the control group. The mean glucose levels in the surgical group fell from 187 mg/dl preoperatively and remained less than 140 mg/dl for up to 10 years of follow-up. The percentage of control subjects being treated with oral hypoglycemics or insulin increased from 56.4% at initial contact to 87.5% at last contact ($P = 0.0003$), whereas the percentage of surgical patients requiring medical management fell from 31.8% preoperatively to 8.6% at last contact ($P = 0.0001$). The mortality rate in the control group was 28% compared to 9% in the surgical group (including perioperative deaths) to be interpreted as follows: for every year of follow-up in this group of T2DM persons, patients in the control group had a 4.5% chance of dying vs. a 1.0% chance for those in the surgical group. The improvement in the mortality rate in the surgical group was primarily due to a decrease in the number of cardiovascular deaths. Mean EWL remained at about 50% over the few years follow-up in the surgical group.

Surgical treatment of obesity and its effect on diabetes: 10-y follow-up. Pories 1992.
Age ≥ 65: Unknown, not in paper
N= 479
M:F: not reported in this article
BMI: All Morbidly Obese
Surgical Type: GBP
Retrospective cohort study

Between 1980 and 1992 Pories et al. (1992) performed the identical Greenville gastric bypass (GGB) procedure on 479 morbidly obese patients with a mortality rate of 1.2%. One hundred and one patients had IGT and 62 had T2DM. The weight loss in the series was well maintained over the follow-up period of 10 years. Of these 163 individuals, 141 reverted to normal (86%) and only 22 (13%) remained with inadequate control of their carbohydrate metabolism. Those patients who were older or whose diabetes was of longer duration were less likely to revert to normal values. The authors concluded that the gastric bypass operation is an effective approach for the treatment of morbid obesity and controls the hyperglycemia, hyperinsulinemia, and insulin resistance of the majority of patients with either glucose impairment or frank NIDDM.

Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. Pories 1995.
Age ≥ 65: None
N= 608
M:F: 102:506
BMI: Mean 49.7 Range (33.9-101.6)
Surgical Type: GBP
Retrospective cohort study

This was a follow-up article to Pories (1992) with an additional 129 patients. One hundred and forty six patients had NIDDM and 152 had IGT. Within these subgroups, 82.9% of NIDDM patients and 98.7% of IGT patients maintained normal levels of plasma glucose, glycosylated hemoglobin, and insulin. The authors believed that these antidiabetic effects appeared to be due primarily to a reduction in caloric intake, suggesting that insulin resistance was a secondary protective effect rather than the initial lesion. In addition to the control of weight and NIDDM, gastric bypass also corrected or alleviated a number of other comorbidities of obesity, including hypertension, sleep apnea, cardiopulmonary failure, arthritis, and infertility. Gastric bypass was now established as an effective and safe therapy for morbid obesity and its associated morbidities. The authors stated that no other therapy has produced such durable and complete control of diabetes mellitus.

Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. Schauer 2003.

Age ≥ 65: Yes, number not reported Range 26-67
N= 1160
M:F: 25:75%
BMI: 50.4 ± 8.5
Surgical Type: LRYGBP
Retrospective cohort study

Schauer et al. (2003) aimed at evaluating pre- and postoperative LRYGBP demographics, duration of diabetes, metabolic parameters, and clinical outcomes, in all patients with impaired fasting glucose (IFG) and type T2DM undergoing the procedure from July 1997 to May 2002. The goal was to follow diabetes status for at least four years after laparoscopic Roux-en-Y gastric bypass (LRYGBP). During this five-year period, 1160 patients underwent LRYGBP and 240 (21%) had IFG or T2DM. Follow up was possible in 191 of the 240 diabetic patients (80%). There were 144 females (75%) with a mean preoperative age of 48 years (range, 26-67 years). After surgery, weight and body mass index decreased from 308 lbs and a BMI of 50.1 to 211 lbs and a BMI of 34 kg/m2 for a mean weight loss of 97 lbs and mean excess weight loss of 60%. Fasting plasma glucose and glycosylated hemoglobin concentrations returned to normal levels (83%) or markedly improved (17%) in all patients. A significant reduction in use of oral antidiabetic agents (80%) and insulin (79%) followed surgical treatment. Patients with the shortest duration (< five years), the mildest form of T2DM (diet controlled), and the greatest weight loss after surgery were most likely to achieve complete resolution of T2DM. The authors concluded that LRYGBP resulted in significant weight loss (60% percent of excess body weight loss) and resolution (83%) of T2DM. Patients with the shortest duration and mildest form of T2DM had a higher rate of T2DM resolution after surgery, suggesting that early surgical intervention is warranted to increase the likelihood of rendering patients euglycemic. No separate analysis of patients aged ≥ 65 was reported.

Outcomes after laparoscopic Roux-en-Y gastric bypass for morbid obesity. Schauer 2000.
Age ≥ 65: Yes number not given. Range 17-68
M:F: 25:75%
BMI: 48.2, Range 35-68
Surgical Type: LRYGBP
Retrospective cohort study

Schauer et al. (2000) evaluated short-term outcomes for laparoscopic Roux-en-Y gastric bypass in 275 patients with a follow-up of one to 31 months with a focus on the benefits of laparoscopic surgery. Consecutive patients (n = 275) who met NIH criteria for bariatric surgery were offered laparoscopic Roux-en-Y gastric bypass between July 1997 and March 2000. A 15-mL gastric pouch and a 75-cm Roux limb (150 cm for superobese) was created using five or six trocar incisions. Twenty-two patients had NIDDM. The incidence of early major and minor complications was 3.3% and 27%, respectively. One death occurred related to a pulmonary embolus (0.4%). Excess weight loss at 24 and 30 months was 83% and 77%, respectively. In patients with more than one year of follow-up, most of the comorbidities were improved or resolved and 95% reported significant improvement in quality of life. In particular, 82% of the NIDDM cases were resolved and the other 18% were improved after surgery.

Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. Sjostrom 2004 NEJM.
Age ≥ 65: None.
N= 1703
M:F: 510:1193
BMI: 40.5± 4.2
Surgical Type: VGB, GBP
Randomized controlled trial

Sjostrom (2004) looked at data from the prospective, controlled Swedish Obese Subjects (SOS) Study which involved obese subjects who underwent gastric surgery and contemporaneously matched conventionally treated obese control subjects with an eye towards measuring the duration of interventions on permanent normalization of serum glucose, triglyceride, and cholesterol levels in patients.

The authors reported follow-up data for subjects (mean age, 48 years; mean body-mass index, 41) who had been enrolled for at least two years (4047 subjects) or 10 years (1703 subjects) before the analysis (January 1, 2004). The follow-up rate for laboratory examinations was 86.6% at two years and 74.5% at 10 years. After two years, the weight had increased by 0.1% in the control group and had decreased by 23.4% in the surgery group ($p< 0.001$). After 10 years, the weight had increased by 1.6% and decreased by 16.1% respectively ($p< 0.001$). Energy intake was lower and the proportion of physically active subjects higher in the surgery group than in the control group throughout the observation period. Two- and 10-year rates of recovery from diabetes, hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, hypertension, and hyperuricemia were more favorable in the surgery group than in the control group, whereas recovery from hypercholesterolemia did not differ between the groups. The surgery group had lower two- and 10-year incidence rates of diabetes, hypertriglyceridemia, and hyperuricemia than the control group; differences between the groups in the incidence of hypercholesterolemia and hypertension were undetectable.

The authors concluded that, as compared with conventional therapy, bariatric surgery appeared to be a viable option for the treatment of severe obesity, resulting in long-term weight loss, improved lifestyle, and, except for hypercholesterolemia, amelioration in risk factors that were elevated at baseline including diabetes and its incidence.

Differentiated long-term effects of intentional weight loss on diabetes and hypertension. Sjostrom 2000.
Age ≥ 65: None
N= 692
M:F: 242:450

BMI: 41.2± 4.7
Surgical Type: VGB, GBP
Randomized controlled trial

As part of the SOS, Sjostrum et al. (2000) wrote a paper on the duration of large maintained weight losses over long periods (> 4 years) after weight loss surgery. They matched 346 patients awaiting gastric surgery with 346 obese control subjects on 18 variables by a computerized matching program. The controls were drawn from a registry consisting of 1508 obese potential controls examined at primary health care centers in Sweden. Of the 692 selected patients (body mass index 41.2± 4.7 $kg/^2$ [mean ± SD]), 483 (70%) were followed for eight years.

No significant weight changes occurred in the obese control group over 8 years. Gastric surgery resulted in a maximum weight loss of -31.1± 13.6 kg after 1 year. After 8 years, the maintained weight loss was still 20.1± 15.7 kg (16.3± 12.3%). Though this weight reduction had a dramatic effect on the eight-year incidence of diabetes (odds ratio 0.16, 95% CI 0.07 to 0.36), it had no effect on the eight-year incidence of hypertension (odds ratio 1.01, 95% CI 0.61 to 1.67). A differentiated risk factor response was identified: a maintained weight reduction of 16% strongly counteracted the development of diabetes over eight years but showed no long-term effect on the incidence of hypertension.

Roux-en-Y gastric bypass versus a variant of biliopancreatic diversion in a non-superobese population: prospective comparison of the efficacy and the incidence of metabolic deficiencies. Skroubis 2006.
Age ≥ 65: None
N= 130
M:F: 26:104 = in each group
BMI: Range 35-50
Surgical Type: RYGBP and BPD-RYGBP
Prospective non-randomized control study

Skroubis et al. (2006), in a prospective comparison of Roux-en-Y gastric bypass (RYGBP) and a variant of biliopancreatic diversion (BPD) in an obese population (BMI 35-50) and from a cohort of 130 patients, randomly selected 65 patients to undergo RYGBP and 65 to undergo BPD. There were 10 diabetics in both groups. All patients underwent complete follow-up evaluation at one, three, six, and 12 months postoperatively and every year thereafter. Patients in both groups completed their second postoperative year. Mean % excess weight loss (%EWL) was significantly better after BPD at all time periods (12 months, p= 0.0001 and 24 months, p= 0.0003), and the %EWL was > 50% in 100% of BPD patients as compared to 88.7% in the RYGBP patients at two-year follow-up. No statistically significant differences were observed between the two groups in early and late non-metabolic complications. Hypoalbuminemia occurred in only one patient (1.5%) after RYGBP and in six patients after BPD (9.2%). Only one patient from each group was hospitalized and received total parenteral nutrition. Glucose intolerance, hypercholesterolemia, hypertriglyceridemia and sleep apnea completely resolved in all patients in both groups. There was no mortality.

The authors concluded that both RYGBP and BPD were safe and effective procedures when offered to these obese patients. Weight loss after BPD was consistently better than that after RYGBP, as was the resolution of diabetes and hypercholesterolemia. Because the nutritional deficiencies that occurred following this type of BPD were not severe and were not significantly different between the two operations, both may be offered to obese patients, keeping in mind the severity and type of preoperative co-morbidities as well as the desired weight loss.

Diabetes and hypertension in severe obesity and effects of gastric bypass-induced weight loss. Sugerman et al. 2003 Ann Surg.
Age ≥ 65: Yes, number unknown. Range 12-69
N= 1025
M:F: 226:799
BMI: African Americans 54 ± 10, Caucasians 49 ± 10
Surgical Type: GBP
Retrospective cohort study

In 2003, a Sugerman study evaluated the preoperative relationships of hypertension and type 2 diabetes mellitus in severe obesity and the effects of gastric bypass (GBP)-induced weight loss. Using the database of patients who had undergone GBP by one general surgeon at a university hospital between September 1981 and January 2000, patient weight, body mass index (BMI), pre- and postoperative diabetes, hypertension, and other comorbidities (sleep apnea, hypoventilation, gastroesophageal reflux, degenerative joint disease, urinary incontinence, venous stasis, and pseudotumor cerebri) were evaluated.

Of 1,025 patients treated (75%W, 25%AA), 15% had pre-op type 2 diabetes mellitus and 51% had hypertension. Of those with diabetes, 75% also had hypertension. Patients who had neither diabetes nor hypertension were younger than those with either diabetes or hypertension, who were younger in turn that those with both diabetes and hypertension. At one year after GBP (91% follow-up), patients lost 66 ± 18% excess weight (%EWL) or 35 ± 9% of their initial weight (%WL). Hypertension resolved in 69% and diabetes in 83%. African-American patients had a higher risk of hypertension than whites before GBP and were less likely to correct their hypertension after GBP. There was significant resolution of other obesity comorbidity problems. At five to seven years after GBP (50% follow-up), %EWL was 59 ± 24 and %WL was 31 ± 13; resolution of hypertension was 66% and diabetes 86%. Of note was that African Americans had a similar of resolution of their T2DM as did whites. No analysis results for patients aged ≥65 were reported.

Effects of bariatric surgery in older patients. Sugerman 2004 Ann Surg.
Age ≥ 65: Yes, mean 63±3. Range 60.1–74.5 years

N= 80
M:F: 18:62
BMI: 49 ± 7
Surgical Type: VBG 1982-1985, GBP thereafter
Retrospective cohort study

Sugerman (2004) utilized a database of patients who had undergone bariatric surgery since 1980 and the National Death Index to do a retrospective cohort evaluation of the safety and efficacy of bariatric surgery in older patients, comparing those < 60 and those ≥ 60 years of age. GBP was the procedure of choice after 1985, VBG before. Data evaluated at one and five years included weight lost, % weight lost (%WL), % excess weight loss (%EWL), % ideal body weight (%IBW), mortality, complications, and obesity comorbidity. The diagnosis of type 2 diabetes mellitus (DM) required an elevated fasting blood sugar (≥150 mg/dL) and either a “diabetic diet” recommended by their primary care physician, oral hypoglycemic medications, or insulin treatment.

A total of eighty patients ≥ age 60 underwent bariatric surgery. They had a mean age of 63 ± 3 years, 78% women, 68 white, 132 ± 22 kg, BMI 49 ± 7 kg/m, 217 ± 32%IBW. Preoperative comorbidity, was greater ($p < 0.001$) in patients ≥ 60 years. There were no perioperative deaths but there were 10 late deaths, 18 months to 10 years (4.5 ± 2.7 years), after bariatric surgery in the older patients. Authors were unable to determine the cause of death in these patients.

Preoperatively, of those patients ≥60 years versus < 60 years diagnosed as having type 2 DM, 42% versus 31% required insulin for control and 20% versus 45% required an oral agent ($p < 0.001$). Pre-operatively 49% of those ≥60 years versus 17% of those < 60 years had a diagnosis of DM and one year after surgery these numbers had improved to show only 17% of those ≥60 years had a diagnosis of DM versus 4% of those < 60 years.

Complications included four major wound infections, two anastomotic leaks, 10 symptomatic marginal ulcers, five stomal stenoses, three bowel obstructions, 26 incisional hernias (non-laparoscopic), and one pulmonary embolism. At one year after surgery (94% follow-up), patients lost 38 ± 11 kg, 57%EWL, 30%WL, BMI 34.5 ± 7 kg/m, %IBW 153 ± 31.

Comorbidities decreased ($p < 0.001$); however, %WL and %EWL and improvement in hypertension and orthopedic problems, although significant, were greater in younger patients. At five years after surgery (58% follow-up), they had lost 31 ± 18 kg, 50%EWL, 26%WL, BMI 35 ± 8 kg/m, and %IBW 156 ± 36.

The authors concluded that bariatric surgery was effective for older patients with a low morbidity and mortality including the resolution of comorbidities. Older patients had more pre- and post-operative comorbidities and lost less weight than younger patients.

Is Roux-en-Y gastric bypass surgery the most effective treatment for type 2 diabetes mellitus in morbidly obese patients? Torquati 2005.
Age ≥ 65: None
N= 96
M:F: 18:79
BMI: 49 ± 7.4
Surgical Type: LRYGBP
Prospective cohort study

The aim of this study by Torquati et al. (2005) was to analyze the effects of RYGB surgery on the glucose metabolism in morbidly obese patients with T2DM. The authors stated that T2DM has a very strong association with obesity. One hundred seventeen morbidly obese patients with T2DM underwent measurements of fasting serum glucose and glycosylated hemoglobin (HbA1C) at baseline before surgery and at six months and 12 months after laparoscopic RYGB surgery. Logistic regression was used in both univariate and multivariate modeling to identify independent variables associated with complete resolution of T2DM. Twelve months after surgery, fasting plasma glucose decreased from a preoperative mean of 164 ± 55 mg/dL to 101 ± 38 mg/dL (P = .001) and HbA1C decreased from a preoperative mean of 7.7% ± 1.5% to 6.0% ± 1.1% (P = .001). Resolution of T2DM was achieved in 72 of the 117 patients (74%). All of the remaining 25 patients decreased the daily T2DM medication requirements. On univariate analysis, preoperative variables associated with resolution of T2DM were waist circumference, HbA1C, and absence of insulin treatment. Waist circumference (odds ratio 2.4; 95% confidence interval 1.4 -4.1; P = .001) and treatment without insulin (odds ratio 42.2; 95% confidence interval 4.3-417.3; P = .002) remained significant predictors of T2DM resolution in the multivariate logistic regression model after adjusting for covariates.

The authors concluded that laparoscopic RYGBP resulted in significant resolution of T2DM. Peripheral fat distribution (smaller waist circumference) and absence of insulin treatment were independent and significant predictors of complete resolution of T2DM.

Short-term effects of sleeve gastrectomy on type 2 diabetes mellitus in severely obese subjects. Vidal 2007.
Age ≥ 65: None
N= 85
M:F: 34:51
BMI: 52.0 ± 1.2 LSG, 47.6 ± 0.7 LRYGBP

Surgical Type: LSG vs LRYGBP
Prospective cohort study

Because data on the effectiveness of sleeve gastrectomy (SG) in improving or resolving type 2 diabetes mellitus (T2DM) are scarce, Vidal et al. (2007) undertook a four-month prospective study on the changes in glucose homeostasis in 35 severely obese T2DM subjects undergoing laparoscopic SG (LSG) and 50 T2DM additional subjects undergoing laparoscopic Roux-en-Y gastric bypass (LRYGBP), matched for DM duration, type of DM treatment, and glycemic control. At four months after surgery, LSG and LRYGBP subjects lost a similar amount of weight (respectively, 20.6 ± 0.7% and 21.0 ± 0.6%). T2DM had resolved respectively in 51.4% and 62.0% of the LSG and LRYGBP subjects (P = 0.332). A shorter preoperative DM duration ($p< 0.05$), a preoperative DM treatment not including pharmacological agents, and a better pre-surgical fasting plasma glucose ($p< 0.01$) or HbAlc ($p< 0.01$), were significantly associated with a better type 2 DM outcome in both surgical groups. The authors concluded that LSG and LRYGBP result in a similar rate of type 2 DM resolution at four months after surgery. Moreover, mechanisms beyond weight loss may be implicated in DM resolution following LSG and LRYGBP.

Long-term outcomes after gastric bypass. White 2005.
Age ≥ 65: Yes number not given Range 18-68
N= 342
M:F: 81:261
BMI: 46.2 ± 9.2 Range 28-99
Surgical Type: GBP
Retrospective Cohort

With an aim of examining long-term follow-up after gastric bypass surgery, White et al.(2005), in New Zealand, studied 342 severely obese patients who underwent gastric bypass between June 1990 and April 2003 by a single surgeon. Careful preoperative documentation and follow-up were maintained on a computerized database. Some late follow-up information was obtained by mailed questionnaire and blood tests. Follow-up data was available for 88% of patients. Follow-up time ranges from 0-14 years, with a median of 48.6 months. Of those lost to follow-up, only 24 (7%) had < 12 months follow-up. The series included 261 females and 81 males. Preoperative BMI ranged from 28-99 (median 44). Before surgery, hypertension was present in 138, type 2 diabetes in 62 (18%), and dyslipidemia in 265. There was no 30-day peri-operative mortality. Three life-threatening complications occurred. BMI and % excess weight loss after one, two, five and 10 years were 28.7 and 89%, 28.3 and 87%, 31.2 and 70% and 31, and 75%, respectively. At last follow-up, 62% of those with hypertension before surgery were cured and 25% had improved. Eighty-five percent of those with type 2 diabetes were cured and 10% had improved. No patients with impaired glucose tolerance had progressed to diabetes. Thirty-four percent of those with dyslipidemia were cured and 38% had improved. No separate analysis data for persons ≥ 65 were reported.

Loss of insulin resistance after Roux-en-Y gastric bypass surgery: a time course study. Wickremesekera 2005.

Age ≥ 65: Yes, Number not given, Range 21-68
N= 71
M:F: 24:47
BMI: Median 45, Range 34-99
Surgical Type: RYGBP
Retrospective cohort

Gastric bypass has repeatedly been shown to improve and even cure T2DM by substantially improving insulin resistance though the mechanism by which it achieves this is not currently known. Wickremesekera et al. (2005) aimed to obtain a better understanding of the time course of the changes in insulin resistance after surgery. He and his colleagues studied 71 patients with and without T2DM diabetes [31 type 2 diabetics (9 insulin-dependent, 11 on oral hypoglycemic agents, 2 diet controlled, 9 previously unrecognized), 11 with impaired glucose tolerance and 29 with normal glucose tolerance] all who had had RYGBP. Insulin resistance was assessed in the 71 patients undergoing gastric bypass surgery by the homeostasis model assessment (HOMA) method before surgery, and again at six days, three, six, nine, and 12 months. Patients were divided into three groups for analysis: diabetics, impaired glucose tolerance and normal glucose tolerance.

All three groups of patients were noted to have insulin resistance prior to surgery. This was greatest in the diabetic patients, as indicated by HOMA. There was marked loss of/improvement in insulin resistance within six days of gastric bypass by both IVGTT and HOMA methods in all groups, which was maintained over the 12-month period. Only three of the 31 diabetic patients on insulin required medication following hospital discharge.

The authors concluded that the changes in insulin resistance seen after gastric bypass, which are responsible for the resolution or improvement of T2DM occur within six days of the surgery, before any appreciable weight loss has occurred.

Health Outcomes of Severely Obese Type 2 Diabetic Subjects 1 Year After Laparoscopic Adjustable Gastric Banding. Dixon 2002.
Age ≥ 65: Unknown, not in paper
N = 500
M:F: 170:330
BMI: 38.7± 6 kg/
Surgical Type: LAGB
Prospective cohort study

To prospectively examine the effect of weight loss one year after laparoscopic adjustable gastric band surgery on a broad range of health outcomes in diabetic subjects, 50 (17 men, 33 women) of 51 patients with type 2 diabetes were selected by Dixon (2002), from a total of 500 consecutive bariatric surgery (LAGB) patients and were studied preoperatively and again one year postoperatively. Preoperative weight and BMI (means ±SD) were 137±30 kg and 48.2±8 kg/m^2, respectively. At one year, weight and BMI were 110± 24 kg and 38.7± 6 kg/m^2, respectively, amounting to 62.5% of EWL in the surgical group as compared with 4.3% in the control group. There was significant improvement in all measures of glucose metabolism. Remission of diabetes, as defined by normal fasting plasma glucose, HbA1c, fasting insulin, and C-peptide, occurred in 32 patients (64%), and major improvement of glucose control occurred in 13 patients (26%). Glucose metabolism was unchanged in five patients (10%). HbA1c was 7.8 ± 3.2% preoperatively and 6.2± 2.7% at one year ($p< 0.001$). Risk factors for remission of diabetes was predicted by logistic regression to be greater weight loss and a shorter history of diabetes (pseudo $r^2= 0.44$, $p< 0.001$). Improvement in diabetes was related to increased insulin sensitivity and β-cell function. The authors concluded that modern laparoscopic weight-loss surgery was effective in managing the broad range of health problems experienced by severely obese individuals with type 2 diabetes and that bariatric surgery should be considered as an early intervention.

Effect of Lap-Band-induced weight loss on type 2 diabetes mellitus and hypertension. Ponce 2004

Age ≥ 65: N. 18-68, mean 41
N= 840
M:F: 143:697
BMI: Mean 48.7, no standard deviation given
Surgical Type: LAGB
Retrospective cohort study

In this study by Ponce et al. (2004) of 840 potential post operative LAGB patients, the primary goal was to measure improvement in diabetes and hypertension comorbidities after surgically-induced weight loss has been documented. Of 840 patients who underwent Lap-Band, data were available in 402 out of 413 patients whose surgery took place at ≥ one year prior. Preoperative and follow-up data were studied retrospectively to examine the effect of Lap-Band induced weight loss on diabetes and hypertension.

Of 413 patients with at least one year postoperative follow-up, 53 (12.8%) were taking medications for type 2 diabetes preoperatively and 66% (n= 35) of diabetic patients were also hypertensive. Resolution of diabetes was observed in 66% at 1 year and 80% at two year follow-up. HbA1c dropped from 7.25% (5.6-11.0, n= 53) preoperatively to 5.58% (5.0-6.2, n= 15) at two years after surgery. Percent excess weight loss (%EWL) was lower for diabetic patients than for the cohort population (39.2% vs 41.2% at one year, 46.7% vs 54.2% at 18 months, and 52.6% vs 63.3% at two years, respectively). Patients in whom diabetes was improved but not resolved had lower %EWL than did those whose diabetes went into remission (27.0% at 1 year and 26.5% at two years). Patients with the shortest duration of diabetes (< 5 years) and better weight loss after surgery achieved higher resolution rates.

The authors concluded that marked improvement in and frequent resolution of diabetes and hypertension were observed as a result of weight loss after Lap-Band surgery.

Laparoscopic adjustable gastric banding for the treatment of morbid (grade 3) obesity and its metabolic complications: a three-year study. Pontiroli 2002.

Age ≥ 65: None
N= 143
M:F: 27:116
BMI: 44.9 ± 0.53
Surgical Type: LAGB vs standard dietary treatment
Retrospective cohort comparison

In a retrospective cohort comparison study of LAGB for treatment of morbid obesity by Pontiroli et al. (2002), 143 patients with grade 3 obesity (27 men and 116 women; mean age 42.9 ± 0.83 yr; mean BMI 44.9 ± 0.53 kg/m^2) underwent LAGB and a three-yr follow-up for clinical (BMI, waist circumference, waist to hip ratio, and arterial blood pressure) and metabolic variables (glycosylated hemoglobin, fasting insulin and glucose, insulin and glucose response to oral glucose tolerance test, homeostasis model assessment index, total and high-density lipoprotein cholesterol, triglycerides, uric acid, and transaminases). Seventy-seven had normal glucose tolerance, 47 had IGT and 19 had T2DM. At baseline and one year after LAGB, patients underwent computerized tomography and ultrasound evaluation of visceral and adipose tissue. One-year metabolic results were compared with 120 obese patients (51 men and 69 women; age, 42.9 ± 1.11 yr; BMI, 43.6 ± 0.46 kg/m^2) where 66 had normal glucose tolerance, eight had IGT, and 46 had T2DM, n = 46. Each received standard diabetic treatment.

For patients having had LAGB, the surgery induced a significant and persistent weight loss and decrease of blood pressure. Greater metabolic effects were observed in T2DM patients (HbA1c reduced from > 8 to 5.5) than in NGT and IGT patients after surgery, so that at three years glycosylated hemoglobin was no longer statistically different in NGT and T2DM subjects, implying resolution of DM. Clinical and metabolic improvements were proportional to the amount of weight loss. With regards to LAGB-treated as compared to diet-treated patients, and at one-year evaluation, weight loss and metabolic improvements were also significantly greater in the LAGB group.

The authors concluded that LAGB was an effective treatment of grade 3 obesity in inducing long-lasting reduction of body weight and arterial blood pressure, modifying body fat distribution, and improving glucose and lipid metabolism, especially in T2DM.

Laparoscopic gastric banding prevents type 2 diabetes and arterial hypertension and induces their remission in morbid obesity: a 4-year case-controlled study. Pontiroli 2005.
Age ≥ 65: None
N= 85
M:F: 13:72
BMI: 45.7 ± 0.67
Surgical Type: LAGB
Retrospective cohort comparison

Pontiroli et al. (2005) performed what they described as a four-year case-controlled study comparing laparoscopic adjustable gastric banding (LAGB) and conventional diet (No-LAGB) in a two-part study. The first part was the prevention (primary intervention study) which studied 56 persons having LAGB and comparing them to 29 persons not having LAGB. These two groups were compared for incidence of T2DM. The second part was a study of DM remission, a secondary intervention study, that included 17 persons with T2DM having LAGB and 20 patients with T2DM not having LAGB. The subjects (n = 122; age 48.5 ± 1.05 years; BMI 45.7 ± 0.67 kg/m2) underwent a diagnostic workup, including psychological and psychiatric assessments, in preparation for the LAGB procedure. Of the 122 subjects, 73 (56+17) had the surgery (LAGB group). The control group (No-LAGB group) consisted of a total of 49 subjects, 29 not having T2DM and 20 that had T2DM. This control group consisted of persons who refused the surgery but agreed to be followed up. The two groups were similar on major demographics and on their glucose status. Six of these subjects dropped out by the second year of the study, so that the final number of patients was 73 and 43 in the LAGB and No-LAGB groups, respectively. All patients had a yearly visit with oral glucose tolerance test.

From baseline to the end of the four-year follow-up, BMI decreased from 45.9 ± 0.89 at baseline to 37.7 ± 0.71 kg/m2 in the LAGB group and remained steady in the No-LAGB group (from 45.2 ± 1.04 to 46.5 ± 1.37 kg/m2), with no significant differences between the primary and secondary intervention groups. In the primary intervention study, five of the No-LAGB subjects (17.2%) and none of the LAGB subjects (0.0%; P = 0.0001) progressed to type 2 diabetes. In the secondary intervention study, type 2 diabetes remitted in one No-LAGB patient (4.0%) and seven LAGB patients (45.0%; P = 0.0052). Hypertension occurred in 11 No-LAGB patients (25.6%) and one LAGB patient (1.4%; P = 0.0001) and remitted in one No-LAGB (2.3%) and 15 LAGB patients (20.5%; P = 0.0001). A study of body mass composition revealed a significant reduction of fat mass and a transitory, but not significant, decrease of fat-free mass in LAGB patients.

The authors concluded that in morbid obesity, sustained and long-lasting weight loss obtained through LAGB prevented the occurrence of type 2 diabetes and hypertension and decreased the prevalence of these disorders by causing resolution through bariatric surgery.

Biliopancreatic diversion with duodenal switch. Marceau 1998.
Age ≥ 65: Number not reported. Range 15-66
N= 252

M:F: 50:202
BMI: DG 46± 9, BPD 47± 9
Surgical Type: BPD, DG
Retrospective cohort study

In 1990, Scopinaro's technique of biliopancreatic diversion (BPD) with distal gastrectomy (DG) and gastroileostomy was modified. A sleeve gastrectomy with duodenal switch (DS) was used instead of the distal gastrectomy and the length of the common channel was made 100 cm instead of 50 cm. BMI's pre-op averaged ≥46. In this study, a questionnaire and a prescription for blood work were sent to 252 patients who underwent DG a mean 8.3 years prior (range 6-13 years) and 465 patients who underwent DS 4.1 years prior (range 1.7-6.0 years). The questionnaire response rate was 93%, and laboratory work was completed for 65% of both groups. The mean weight loss after DG was 37 ± 21 kg and after DS 46 ± 20 kg. About 74% of the patients after DG and 87% of patients after DS had lost more than 50% of their initial excess weight (EWL). The two procedures were equally efficient for treating the co-morbid conditions of diabetes. After the procedures, 69 of 72 (96%) diabetic patients no longer required medical treatment. The authors concluded that BPD or DG can cure T2DM. No separate analysis was reported for persons ≥ 65.

Type 2 diabetes and weight loss following biliopancreatic diversion for obesity. Marinari 2006.
Age ≥ 65: None
N= 268
M:F: 102:166
BMI: 49.6 ± 0.48
Surgical Type: BPD
Retrospective matched cohort study

Marinari et al.(2006) studied the weight loss and maintenance in type 2 diabetic obese patients undergoing biliopancreatic diversion (BPD). Two series of diabetic and non-diabetic obese patients, 268 in each group, were matched for gender, age and baseline body mass index (BMI ranged from 36 -72) and preoperatively their average blood glucose was 178 as compared with 95 for the non-diabetic obese patients. In preop diabetic subjects, mean values of BW and BMI were not significantly different from those of non-diabetic subjects. The subjects were evaluated prior to BPD, on the occasion of the regular follow-up visit at one, two and three years following the operation, and at the fifth postoperative year. At three years of follow-up, 261 were available in the surgical group and 255 were available in the matched group. At each follow-up point, BW, BMI, and serum glucose concentration were measured.

In 100% of the T2DM patients, the serum glucose level fell to within the normal range at the first postoperative year and remained within normal limits without any medication throughout all the follow-up periods.

GLP-1 and changes in glucose tolerance following gastric bypass surgery in morbidly obese subjects. Morinigo. 2006.

Age ≥ 65: None
N= 34
M:F: 23:11
BMI: 49.1± 1.0
Surgical Type: BPD
Prospective cohort study

To examine the proposition that dramatic improvement of type 2 diabetes following RYGBP could by accounted for, at least in part, by changes in glucagon-like peptide-1 (GLP-1) secretion, Morinigo et al. did a 12-month prospective study on the changes in glucose homeostasis and active GLP-1 in response to a standard test meal (STM) in 34 obese subjects (BMI 49.1± 1.0 kg/^{2}) who had different degrees of glucose tolerance: normal glucose tolerance (NGT, n= 12), impaired glucose tolerance (IGT, n= 12), and type 2 diabetes (n= 10).

At six weeks after RYGBP, despite the subjects still being markedly obese (BMI 43.5± 0.9 kg/^{2}), fasting plasma glucose and HbA1c decreased in the study groups ($p< 0.05$). Insulin sensitivity improved, but was still abnormal in a comparable proportion of subjects among groups ($p= 0.717$). When insulin secretion was adjusted for the prevailing insulin sensitivity, an increase was found in subjects with diabetes ($p< 0.05$) although it remained lower compared to NGT and IGT subjects ($p< 0.01$). At 12 months follow-up, no differences among groups were found in the evaluated glucose homeostasis parameters. Compared to baseline, at six weeks the incremental AUC of active GLP-1 in response to the STM increased in NGT and IGT ($p< 0.05$) but not in subjects with diabetes ($p= 0.285$). However, the GLP-1 response to a STM was comparable among groups at 12 months follow-up ($p= 0.887$).

The authors concluded that RYGBP was associated with an improvement, but not complete restoration, of glucose homeostasis at six weeks after surgery and that GLP-1 was not a critical factor for the early changes in glucose tolerance.

A comparison of a personal series of biliopancreatic diversion and literature data on gastric bypass help to explain the mechanisms of resolution of type 2 diabetes by the two operations. Scopinaro 2008.
Age ≥ 65: None
N= 443
M:F: 171:272
BMI: 49.9± 9.15
Surgical Type: BPD
Retrospective cohort study

In both RYGBP and BPD, the foregut is excluded from the food stream and the distal small bowel receives the food stimulation; following BPD, fat intestinal absorption is also extremely limited. This study by Scopinaro (2008) was carried out to identify clinical features that could give insight on the different mechanisms of action on diabetes resolution.

The files of 443 severely obese patients with T2DM (of a total of 3020) undergoing BPD from May 1976 to May 2007 were examined, and the presence of T2DM (fasting serum glucose > 125 mg/ml) at one – two months, at one year, at 10 years, and at ≥ 20 years following the operation was recorded. The percentage of patients cured (fasting serum glucose reduced to ≤ 110 mg/dl, on free diet and with no therapy) was 74% at one month, 97% at one and 10 years, and 91% at ≥ 20 years. The 26% of uncured patients at one month had the most severe preoperative T2DM.

The author concluded that as the early results after BPD resemble those reported after RYGBP, it could be hypothesized that the duodenal exclusion and the distal small bowel stimulation were the first mechanisms acting in BPD, immediately after the operation, and that only subsequently the myocellular fat depletion, which cannot be immediate, takes over, and fat absorption was the mechanism accounting for the long-term results of BPD.

Predictors of weight loss and reversal of comorbidities in malabsorptive bariatric surgery. Valera-Mora 2005.
Age ≥ 65: None
N= 107
M:F: 22:85
BMI: Females 48.9 ± 8.8, Males 48.1 ± 6.1
Surgical Type: BPD
Prospective cohort study

The objective of a prospective cohort study by Valera-Mora et al. (2005) was to identify predictors of weight loss and reversal of comorbidity in obese patients undergoing BPD. Morbidly obese men and women (n = 107) were studied before and two years after biliopancreatic diversion (BPD). Body composition, serum lipid profile, oral glucose tolerance, and blood pressure were measured. Insulin sensitivity was determined by use of a euglycemic clamp. The length of the small intestine was measured during surgery. Intestinal length was 671 ± 99 cm, and the residual absorbing intestine after BPD ranged from 54% to 24% of initial length. Patients lost an average of 36% of their initial weight, with approximately 50% of them reaching a BMI < 30. Serum cholesterol decreased (from 4.58 ± 1.11 to 3.34 ± 0.73 mmol/L; $p < 0.0001$), as did serum triacylglycerols (from 1.52 ± 0.59 to 0.88 ± 0.35 mmol/L; $p < 0.0001$), whereas insulin sensitivity rose 150% (from 26 ± 4 to 64 ± 11 micromol $p < 0.0001$). Diabetes (in 23% of patients before surgery) and hypertension (in 83%) were reduced (by 88% and 96%, respectively) after surgery. In a multivariate model (including sex, age, intestinal length, presence of diabetes, insulin sensitivity, and initial fat mass), age and diabetes were independent, negative predictors of weight loss, whereas initial fat mass was a strong positive predictor ($r^2 = 0.51$).

The authors concluded that two years after BPD in morbidly obese patients, comorbidities were largely corrected and insulin resistance was fully reversed despite persistent obesity. Initial fat mass, but not residual intestinal length, was the strongest predictor of weight loss after BPD.

Effectiveness of laparoscopic sleeve gastrectomy (first stage of biliopancreatic diversion with duodenal switch) on co-morbidities in super-obese high-risk patients. Silecchia 2006.

Age ≥ 65: None
N= 41
M:F: 13:28
BMI: 57.3± 6.5
Surgical Type: LSG
Prospective non controlled cohort study

To evaluate the effect of laparoscopic sleeve gastrectomy (LSG) on major co-morbidities (hypertension, type 2 diabetes / impaired glucose tolerance, obstructive sleep apnea syndrome), 41 super-obese high-risk patients (mean BMI 57.3± 6.5 kg/m^2, age 44.6± 9.7 years) were entered into a prospective study. Nine patients had BMI ≥60. Seventeen patients (41.4%) had T2DM or IGT. A number (14) of patients had had unsuccessful prior surgery (LAGB, intragastric balloon). Patients underwent evaluation every three months postoperatively and were restaged at 12 months and/or before the second step. Sixty percent of major co-morbidities were cured and 24% improved. Average BMI after six and 12 months was 44.5± 8.1 and 40.8± 8.5 respectively (mean follow-up 22.2±7.1 months). After 12 months, 57.8% of the patients were co-morbidity-free and 31.5% had only one major co-morbid condition. Three patients had BMI < 30 and were co-morbidity-free 12 months after LSG. There was zero% mortality. Twelve of the 17 (71%) pre-op T2DM or IGT were resolved.

The authors concluded that LSG represented a safe and effective procedure to achieve marked weight loss as well as significant reduction of major obesity-related co-morbidities.

Evidence: BMI < 35

Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. Dixon 2008 JAMA.
Age ≥ 65: None
N= 60
M:F: 30:30
BMI: 30-40, Mean 37
Surgical Type: LAGB
Randomized controlled trial

In early 2008, Dixon et al. did a randomized controlled trial of LAGB versus conventional diabetes care including 60 obese patients (BMI > 30 and < 40 mean 37) with recently diagnosed (< 2 years) type 2 diabetes to determine if surgically induced weight loss resulted in better glycemic control and less need for diabetes medications than conventional approaches to weight loss and diabetes control. This unblinded randomized controlled trial was conducted from December 2002 through December 2006 at the University Obesity Research Center in Australia, using general community recruitment to established treatment programs. Specifically, the interventions compared were conventional diabetes therapy with a focus on weight loss by lifestyle change vs laparoscopic adjustable gastric banding. The main outcome measure was remission of type 2 diabetes (fasting glucose level < 126 mg/dL and glycated hemoglobin [HbA1c] value < 6.2% while taking no glycemic therapy). Secondary outcome measures included weight and components of the metabolic syndrome. Analysis was by intention-to-treat.

Of the 60 patients enrolled, 55 (92%) completed the two-year follow-up. Remission of type 2 diabetes was achieved by 22 (73%) in the surgical group and four (13%) in the conventional-therapy group. Relative risk of remission for the surgical group was 5.5 (95% confidence interval, 2.2-14.0). Surgical and conventional-therapy groups lost a mean (SD) of 20.7% (8.6%) and 1.7% (5.2%) of weight, respectively, at two years ($p < .001$). Remission of type 2 diabetes was related to weight loss ($r^2 = 0.46$, $p < .001$) and lower baseline HbA1c levels (combined $r^2 = 0.52$, $p < .001$). There were no serious complications in either group. According to Dixon (personal communication 8/08), 14 of these patients had a BMI between 30 and 35, of whom seven had surgery with modest results at 24 months in the five that could be followed.

The authors concluded that, overall, participants randomized to surgical therapy were more likely to achieve remission of type 2 diabetes through greater weight loss. These Results need to be confirmed in a larger, more diverse population and have long-term efficacy assessed.

Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program: a randomized trial. O'Brien, 2006.
Age ≥ 65: None
N= 80
M:F: 18:62
BMI 30-34
Surgical Type: LAGB
Randomized controlled trial

Because observational studies suggest that bariatric surgery is more effective than nonsurgical therapy, but no randomized controlled trials have confirmed this, O'Brien et al. did a study aimed at ascertaining whether surgical therapy for obesity achieves better weight loss, health, and quality of life than nonsurgical therapy. The study was performed by a university department of medicine and surgery and an affiliated private hospital.

Eighty adults with mild to moderate obesity (body mass index, 30 kg/m^2 to 35 kg/m^2) from the general community were assigned to a program of very-low-calorie diets, pharmacotherapy, and lifestyle change for 24 months (nonsurgical group) or to placement of a laparoscopic adjustable gastric band.

Outcome measures were weight change, presence of the metabolic syndrome, and change in quality of life at two years. We note that in this article metabolic syndrome was defined by the ATP III criteria and therefore T2DM might not be present in each person in this study with metabolic syndrome. At two years, the surgical group had greater weight loss, with a mean of 21.6% (95% CI, 19.3% to 23.9%) of initial weight lost and 87.2% (CI, 77.7% to 96.6%) of excess weight lost, while the nonsurgical group had a loss of 5.5% (CI, 3.2% to 7.9%) of initial weight and 21.8% (CI, 11.9% to 31.6%) of excess weight ($p< 0.001$). The metabolic syndrome was initially present in 15 (38%) patients in each group and was present in eight (24%) nonsurgical patients and one (3%) surgical patient at the completion of the study ($p< 0.002$). The study was limited by not being powered for comparison of adverse events, and examined outcomes only for 24 months.

The authors concluded that surgical treatment using LAGB was statistically significantly more effective than nonsurgical therapy in reducing weight, resolving the metabolic syndrome, and improving quality of life during a 24-month treatment program.

Laparoscopic adjustable gastric banding for patients with body mass index of <or=35 kg/m^2. Parikh 2006.
Age ≥ 65: Yes Number not given Range 16-76
N= 93
M:F: 17:76
BMI: 30-34
Surgical Type: LAGB
Retrospective cohort study

Between 1996 and 2004 (Parik 2006) studied 93 patients with a BMI of 30-35 kg/m^2 who underwent LAGB out of 3100 total patients with all range of BMIs. All patients were referred by their primary physician, entered into a comprehensive bariatric surgery program at one Australian center, and operated on by one surgeon. Data on all patients were collected prospectively and entered into an electronic registry. The study parameters included preoperative age, gender, BMI, presence of co-morbidities, percentage of excess weight loss, and resolution of co-morbidities.

The mean age was 44.6 years (range 16-76), mean weight was 98 kg, and the mean BMI was 32.7 kg/m^2 (range 30-34). Of the 93 patients, 42 (45%) had co-morbidities, including eight with diabetes. The proportion of patients in follow-up was 79%, 85%, and 89% at one, two and three years, respectively. The mean weight was reduced to 71 kg at one year, 72 kg at two years, and 72 kg at three years. The mean BMI was reduced to 27.2 ± 2.2, 27.3 ± 3.1, and 27.6 ± 3.7 kg/m^2, respectively, and the mean percentage of excess weight loss was 57.9% ± 24.5%, 57.6 ± 29.3%, and 53.8% ± 32.8% at one, two and three years, respectively. At three years, the BMI was 18-24 kg/m^2 in 34%, 25-29 kg/^{2} in 51%, and 30-35 kg/m^2 in 10%. At 3 years, the percentage of excess weight loss was < 25% in 10%, 25-50% in 24%, 50-75% in 51%, and > 75% in 10%. The diabetes completely resolved in all eight patients. No mortality occurred. No results were separately reported for person over the age of 65.

The authors concluded that, with additional study, it was reasonable to expect the weight guidelines for bariatric surgery to be altered to include patients with a BMI of 30-35 kg/m^2.

Duodenal switch without gastric resection: results and observations after 6 years. Cossu 2004.
Age ≥ 65: None
N= 24
M:F: 13:11

BMI: 30-40, Mean 36.2
Surgical Type: BPD-DS w/o gastric resection
Retrospective cohort study

Between 1996 and 1999, Cossu et al. (2004) performed the duodenal switch (DS) without gastric resection on 24 mildly obese patients. Mean preoperative BMI was 36.2 kg/m^2 (BMI 30-40). Seventeen patients (70.8%) suffered from type 2 diabetes: 13 were being treated with oral antidiabetic drugs and/or insulin, and four (16.6%) had impaired glucose tolerance while the remainder (3) had fasting hyperglycemia.

In 20 patients (83.3%), hypercholesterolemia and alterations in lipid profile were present. Another 20 patients were taking drugs for hypertension. The metabolic syndrome was present in 41.6% of patients. Mean follow-up was 4 years.

BMI reduction and weight loss were not large. Two patients who had severe longstanding diabetes type 2 needed a second operation of the classical BPD because of failure in improving diabetes. Another two patients were changed to classical BPD because of a relapsing chronic duodeno-ileal ulcer. The incidence of ileal ulcer was 29.1%.

The authors concluded that, regarding hypercholesterolemia, hypertriglyceridemia, and type 2 diabetes, when there was a good pancreatic "reservoir," the operation seemed effective in the long-term. Protein absorption was better than that obtained with the classical BPD. The authors also concluded that long-term results suggested that in carefully selected patients suffering from serious hypercholesterolemia or type 2 diabetes with insulin reserves still at an acceptable level, and with BMI 30-40, DS without gastric resection can be proposed as a surgical treatment for metabolic diseases but not for obesity. With only 24 patients with different kinds of diabetes and with BMIs ranging far and wide from 24 to over 45, they made questionable conclusions.

Biliopancreatic diversion preserving the stomach and pylorus in the treatment of hypercholesterolemia and diabetes type II: results in the first 10 cases. Noya 1998
Age ≥ 65: None
N= 10
M:F: 5:5
BMI: Mean 33.2
Surgical Type: BPD
Retrospective cohort study

Between March 1996 and July 1997 Noya et al. (1998) performed BPD without gastric resection on 10 moderately overweight patients [mean body mass index (BMI) = 33.2 kg/m^2]. All patients had suffered from hypercholesterolemia and hypertriglyceridemia for more than five years. Ten patients suffered from T2DM, four of them had had insulin treatment or oral anti-diabetic agents; the other patients all had hyperglycemia in the fasted state and diabetes confirmed by preoperative oral glucose tolerance test (OGTT). Five patients suffered from hypertension.

In all patients, cholesterol and triglyceride levels returned to normal within the first postoperative month. Glycemia also stabilized at normal values in nine patients within the early weeks after surgery. One patient who took 70 U of insulin reduced his daily intake to 35 U two months postoperatively. In all patients, blood pressure returned to normal. Weight loss was predictably slight (10-15 kg).

The authors concluded that their experience with the procedure found that this new method seemed to be as effective in controlling lipid metabolism and T2DM as the original version of BPD. As expected, weight loss was only moderate, so they concluded that the modified BPD was not suitable for very obese patients.

Long-term control of type 2 diabetes mellitus and the other major components of the metabolic syndrome after biliopancreatic diversion in patients with BMI < 35 kg/m2. Scopinaro 2007.
Age ≥ 65: None
N= 7
M:F: not reported in paper
BMI: 30-34
Surgical Type: BPD
Retrospective cohort study

Scopinaro (2007) aimed at reinforcing his opinion that bariatric operations were the most powerful means of curing type 2 diabetes mellitus (T2D) and the other major components of the metabolic syndrome and may be considered in patients with BMI's < 35. Despite the very frequent occurrence of metabolic disturbances in patients with BMI from 30 to 35, he noted a general reluctance to operate on these patients, as their disease was considered less severe. Seven T2DM obese patients with mean BMI < 35 underwent BPD between 1976 and 1996 at the Azienda Ospedaliera Universitaria San Martino of Genoa, Italy. Mean age was 49 years, mean body weight 91 kg, and mean waist circumference 115 (M) and 98 (F) cm. The mean follow-up was 13 (10-18) years. All seven patients had abnormally high values of serum triglyceride, serum cholesterol, and arterial pressure.

In all seven patients, serum glucose was normalized at one, two and three years. In five patients, a slight increase of serum glucose above 125 mg/dl was observed at or around five years, the values being maintained at all subsequent times, with no one value higher than 160 mg ever being recorded. The other two patients showed full resolution of diabetes at all follow-up times. Both serum cholesterol and triglyceride values fell to normal one year after BPD, and remained within the normal range in all seven patients during the entire follow-up observation. Arterial pressure normalized in six cases and was improved in one case. No patient had excessive weight loss at any postoperative time.

The authors concluded that T2D patients with BMI < 35 have very severe metabolic disturbances and that surgical therapy for these patients was warranted, and should be performed as soon as possible, before the rapid evolution of the pattern leads them to a point where even the most effective metabolic surgery operation could be insufficient to yield complete and permanent control of their diabetes.

Laparoscopic Roux-en-Y gastric bypass for BMI under 35: A tailored approach. Cohen 2006
Age ≥ 65: None
N= 37
M:F: 7:30
BMI: 32-34
Surgical Type: LRYGBP
Probably Retrospective Cohort- not enough info to determine

Noting that there is a group of patients with BMI under 35 that are obese, have uncontrolled comorbidities, and that have tried to lose weight with no success, Cohen et al, undertook a study of 37 obese patients who were under clinical treatment with no resolution or improvement of their life-threatening comorbidities. These patients were selected for LRYGBP using the following criteria: BMI between 32 and 35 kg/m2; presence of at least three co-morbidities; failure of medical treatments (lifestyle modification and pharmacotherapy); presence of central obesity; and approval by their primary care physician. The patients underwent the same preoperative evaluation as other patients for gastric bypass. The primary care physicians were responsible for the diagnosis of type 2 diabetes mellitus, hypertension, lipid disorder, gastroesophageal reflux disease (GERD), and sleep apnea. Type 2 diabetes was diagnosed if the patient presented with two fasting serum glucose results ≥120 mg/dL. Hypertension was diagnosed if the systolic blood pressure was ≥140 mm Hg and/or the diastolic blood pressure was ≥90 mm Hg.

The mean BMI was 32.5, and there were 30 women and seven men. Ages ranged from 28 to 45. All patients had T2DM, hypertension, and lipid disorder. GERD was present in seven patients and sleep apnea in three. Patients with type 2 diabetes mellitus (37/37) used at least two oral antidiabetic drugs. None of them were using insulin. Patients underwent the same preoperative evaluation as other patients for gastric bypass. Patients were required to have approval by their primary care physician. Written informed consent was obtained from all patients. Laparoscopic Roux-en-Y gastric bypass was performed. After extensive explanation and documentation, Brazilian insurance companies approved the procedure in three cases. International (non-American) insurance companies approved the procedure in four cases. Follow-up ranged from six to 48 months. The mean excess weight loss was 81%. Thirty-six patients (97%) had total remission of their comorbidities. One patient still had mild hypertension but with a reduction in the number of anti-hypertensive drugs. There were no surgery-related complications. Postoperative quality of life was considered good to excellent. The authors concluded that obese patients with BMIs under 35 and with severe comorbidities benefited from laparoscopic Roux-en-Y gastric bypass and that this treatment option should be offered to this group of patients.

Effect of laparoscopic mini-gastric bypass for type 2 diabetes mellitus: comparison of BMI > 35 and < 35 kg/m^2. Lee 2008b.

Age ≥ 65: None
N= 201
M:F: 58:143
BMI: < 35 versus > 35
Surgical Type: Mini RYGBP 201 with T2DM or IGT
Retrospective cohort study

Lee et al. (2007) enrolled and prospectively studied 820 patients who were in a surgically supervised weight loss program between Jan 2002 and Dec 2006 and who underwent laparoscopic mini-gastric bypass. Two hundred one (24.5%) of these patients had impaired fasting glucose or T2DM. Patients with BMI< 35 kg/m^2 were compared with those of BMI> 35 kg/m^2. Successful treatment of T2DM was defined by HbA1C< 7.0%, LDL< 100 mg/dl, and triglyceride< 150 mg/dl.

Among the 201 patients, 44 (21.9%) had BMI< 35 kg/m^2, and 114 (56.7%) had BMI between 35 and 45, 43 (21.4%) had BMI> 45 kg/m2. Patients with BMI< 35 kg/m2 were significantly older, female predominant, had lower liver enzyme and C-peptide levels than those with BMI>35 kg/m^2. The mean total weight loss for the population was 32.1, 33.4, 31.9, and 32.8% (at one, two, three, five years after surgery), and percentage decrease in BMI was 31.9, 34.2, 32.2, and 29.5% atone, two, three and five years. One year after surgery, fasting plasma glucose returned to normal in 89.5% of patients with a BMI< 35 kg/m^2 and 98.5% of patients with a BMI ≥35 kg/m^2 (p= 0.087). The treatment goal of T2DM (HbA1C< 7.0%, LDL< 150 mg/dl and triglyceride< 150 mg/dl) was met in 76.5% of BMI< 35 kg/m2 and 92.4% of BMI> 35 kg/m2 (p= 0.059). There was one death out of 201 patients and that was in one patient with a BMI over 45.

The authors concluded that laparoscopic gastric bypass resulted in significant and sustained weight loss with successful treatment of T2DM up to 87.1%. They also concluded that despite a slightly lower response rate of T2DM treatment, patients with BMI < 35 still had an acceptable T2DM resolution, and this treatment option can be offered to this group of patients.

Laparoscopic treatment of metabolic syndrome in patients with type 2 diabetes mellitus. Depaula AL 2008.
Age ≥ 65: Yes Number not given Range 27-66
N= 60
M:F: 24:36
BMI: mean 30.1 (range 23.6-34.4)
Surgical Type: L Ileal Interposition with LSG in 32, D-SG in 28
Retrospective cohort study

Metabolic syndrome refers to risk factors for cardiovascular disease. Hyperglycemia is a critical component contributing to the predictive power of the syndrome. This study by DePaula et al. (2008) aimed at evaluating the results from the laparoscopic interposition of an ileum segment into the proximal jejunum with LSG for the treatment of metabolic syndrome in patients with type 2 diabetes mellitus and a body mass index (BMI) lower than 35.

Laparoscopic procedures were performed for 60 patients (24 women and 36 men) with a mean age of 51.7 ± 6.4 years (range, 27-66 years) and a mean BMI of 30.1 ± 2.7 (range, 23.6-34.4). All the patients had a diagnosis of T2DM of at least three years duration and evidence of stable treatment using oral hypoglycemic agents, insulin, or both for at least 12 months. The mean duration of T2DM was 9.6 ± 4.6 years (range, 3-22 years). Metabolic syndrome was diagnosed for all 60 patients. Arterial hypertension was diagnosed for 70% of the patients and hypertriglyceridemia for 70%. High-density lipoprotein was altered in 51.7% of the patients and the abdominal circumference in 68.3%. Two techniques were performed: ileal interposition (II) into the proximal jejunum and sleeve gastrectomy (II-SG) or ileal interposition associated with a diverted sleeve gastrectomy (II-DSG).

The II-SG procedure was performed for 32 patients and the II-DSG procedure for 28 patients. The mean postoperative follow-up period was 7.4 months (range, 3-19 months). The mean postop BMI was 23.8 ± 4.1 kg/m^2, and 52 of 60 patients with pre-op T2DM (86.7%) achieved adequate glycemic control. Hypertriglyceridemia was normalized for 81.7% of the patients. A high-density lipoprotein level higher than 40 for the men and higher than 50 for the women was achieved by 90.3% of the patients. The abdominal circumference reached was less than 102 cm for the men and 88 cm for the women. Arterial hypertension was controlled in 90.5% of the patients. For the control of metabolic syndrome, II-DSG was the more effective procedure. There was no mortality. The authors concluded that Laparoscopic II-SG and II-DSG were promising procedures for the control of the metabolic syndrome and type 2 diabetes mellitus and a longer follow-up period was needed. There were no separate analyses for persons ≥65.

No MEDCAC was held on this topic

5. Evidence-based guidelines

We were unable to identify any guidelines on bariatric surgery for the treatment of diabetes in patients with BMI < 35.

6. Expert Opinion

Bariatric surgery: effects on glucose homeostasis. Rubino 2006.
Rubino (2006) wrote a review of the relationship between gastrointestinal anatomy and glucose homeostasis.

Along with sustained body weight loss, all bariatric operations lead to improvement or resolution of comorbid disease states, particularly type 2 diabetes. Roux -en-Y gastric bypass and biliopancreatic diversion are the most effective methods to control diabetes, resulting in persistent normal concentrations of plasma glucose, insulin, and glycosylated hemoglobin in 80-100% of cases. Resolution of diabetes after such treatment typically occurs too fast to be accounted for by weight loss alone. Recent animal investigations using duodenal-jejunal bypass, a stomach-preserving experimental model of Roux-en-Y gastric bypass, have shown that diabetes control is not a mere collateral effect of the treatment of obesity, but directly results from the exclusion of the duodenum and proximal jejunum from the flow of nutrients.

The author concluded that results from clinical series and animal studies suggested that type 2 diabetes was a potentially operable disease. He believes this indicates the need for carefully conducted clinical trials to define the ideal candidate patients and the most suitable type of operation for surgical treatment of type 2 diabetes. The author felt that understanding the exact mechanism by which Roux-en-Y gastric bypass controls diabetes is a priority because such knowledge may help us to understand the relationship between gastrointestinal physiology and insulin resistance as well as to help us identify new targets for novel antidiabetic medications.

Effects of obesity surgery on non-insulin-dependent diabetes mellitus. Greenway 2002.

In a review article of many papers on the effects of obesity surgery on non-insulin-dependent diabetes mellitus by Greenway et al. (2002) which cited 148 references (including older papers and on techniques not in common use now such as VBG bariatric surgical procedures), the authors stated that BS surgical procedures have proven a much more successful method of weight loss and diabetes control in the obese population than conservative methods. The review reported that these surgical procedures have proven safe with reported mortality rates of 0% to 1.5%. The overwhelming consensus was that DM is resolved or improved by BS in the vast majority of patients.

Many of the articles reviewed are included in our evidence summary reported above. Others are not relevant anymore though we have included good data from RCTs such as those from the Swedish SOS.

Obesity, bariatric surgery and type 2 diabetes a systematic review. Ferchak 2004.

Ferchak et al. (2004) undertook a systematic review of the relation between obesity, bariatric surgery and T2DM. The review reiterated that obesity was endemic in the United States and was closely linked to the development of type 2 diabetes; that both obesity and diabetes were responsible for significant morbidity and mortality and that both conditions were resistant to treatment.

They reported that recent studies have evaluated prevention of T2DM through intensive lifestyle intervention, while others examine the impact of bariatric surgery on T2DM. They presented an overview of the impact of bariatric surgical and lifestyle interventions on the prevention and treatment of type 2 diabetes. Although studies using a variety of bariatric surgical techniques were included, the focus was on two interventions in particular: RYGBP and LAGB. Outcomes of these procedures were further contrasted with recent lifestyle intervention studies, in particular, the Diabetes Prevention Program study. The authors reported that gastric bypass studies show that GBP was associated with a 99 to 100% prevention of diabetes in patients with IGT and an 80 to 90% clinical resolution of diagnosed early T2DM. Gastric banding procedures were associated with a lower median (50-60%) clinical remission of T2DM. Lifestyle intervention studies of obese and glucose-intolerant patients have achieved a 50% reduction in the progression of IGT to diabetes over the short term, with no reported resolution of the disease. Weight loss by any means in the obese patient appeared to prevent progression to type 2 diabetes, at least in the short term. Furthermore, sustained weight loss through bariatric surgical intervention was associated both with prevention of progression of IGT and with clinical remission of early T2DM.

7. Public Comments

Public comments sometimes cite the published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

A. Initial Public Comments

CMS received 21 comments during the initial 30-day public comment period. These comments were summarized in the proposed decision memorandum and may be viewed in total by using the following link:
http://www.cms.hhs.gov/mcd/viewpubliccomments.asp?nca_id=219&rangebegin=11%5F17%5F2008&rangeend=12%5F17%5F2008

B. Public Comments on the Proposed Decision

CMS received a total of 26 responses during this comment period. Few respondents commented on both parts of the coverage determination: 1) specification of type 2 diabetes as a comorbidity necessary to qualify for surgery among persons with a BMI $\geq$ 35, and 2) noncoverage of surgery among persons with a BMI < 35. Four of the commenters supported the specification of diabetes as a comorbidity among patients with higher BMI; one party agreed with the noncoverage of surgery among persons with lower BMI; and approximately 20 respondents disagreed with the noncoverage determination among persons of lesser BMI. Of the 20 commenters disagreeing with the noncoverage determination, 13 submitted a version of a standardized form letter.

Comments from Professional Societies and Organizations

Comment: CMS received a combined comment from three professional societies: the American College of Surgeons (ACS); the American Society for Metabolic and Bariatric Surgery (ASMBS); and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). The content of this letter was similar to the form letters regarding the following two points:

1) Ongoing clinical trials will shortly clarify the efficacy and safety of bariatric surgery in patients with type 2 diabetes and a BMI of $\geq$ 30. Concern was expressed that the results of this ongoing/future research may be disregarded by CMS and that a more appropriate coverage determination for persons with BMI < 35 would involve coverage with evidence development.

2) Medicare Administrative Contractors (MACs) may interpret type 2 diabetes as being the only acceptable comorbidity and continue to apply their own additional standards limiting care (e.g., some MACs require Medicare beneficiaries to have uncontrolled type 2 diabetes in order to qualify as an acceptable candidate for bariatric surgery). It was suggested that CMS issue specific instructions informing MACs that the diagnosis of type 2 diabetes in any morbidly obese individual is only one of many acceptable comorbidities enumerated in the February 21, 2006 NCD.

A final point raised by these commenters, not included among the form letters, was that the proposed coverage determination fails to treat obesity "as a disease," contains arbitrary boundaries and indications for treatment, "perpetuates the myth that somehow obesity treatment requires a different set of rules," and "reinforces the discriminatory and prejudicial treatment of obese patients by other national and state insurers and employers."

Response: CMS believes that the evidence does not warrant a decision using coverage with evidence development. CMS is eager to review the results of ongoing trials as they are published in the literature and could reconsider an NCD based on such a publication.

This coverage determination does not limit other comorbidities that may be used by contractors to permit coverage of bariatric surgery, it merely specifies type 2 diabetes as one such comorbidities.

CMS has existing policy that explains why we do not consider obesity a disease, which is outside the scope of this decision.

Comment: The Endocrine Society supported the CMS decision to specify type 2 diabetes as a comorbidity for determining the appropriateness of bariatric surgery among persons with a BMI $\geq$ 35 but expressed concern with the non-coverage recommendation for persons with type 2 diabetes and a BMI < 35.

It was the opinion of the Society that a non-coverage decision based upon the current lack of evidence supporting the benefits of surgery among persons of lesser BMI is premature and might impair the ability to recruit for and to conduct studies that might provide confirmatory evidence.

Therefore, the Society suggested that CMS refrain from making any formal conclusion in the NCD about patients with Type 2 DM and BMI < 35. This type of decision would afford the opportunity to conduct the studies that might provide the data necessary for a positive coverage determination assuming adequate data became available.

Response: CMS may only cover those items and services that are shown to be reasonable and necessary, based upon consideration of the available evidence. Parties are free to conduct research that may provide evidence to reverse a non-coverage determination but CMS is not obligated to support such research.

Comment: A consensus statement from the “First International Conference on Gastrointestinal Surgery to Treat Type 2 Diabetes (Diabetes Surgery Summit [DSS])” – held in Rome in March 2007 (to be published in 2009) was submitted, and the commenter concurred that sufficient data did not yet exist to support a positive coverage determination among persons with a BMI < 35 but questioned whether a somewhat arbitrary BMI cut-point is a valid criterion for making the decision whether surgery is beneficial. The commenter suggested that a more reasonable approach would be to establish a comprehensive risk/benefit profile of individual patients, and consider a surgical option in those with inadequately controlled T2DM and at high cardiovascular risk due to their metabolic status.

Response: CMS based its coverage determination, in part, on the BMI cut-point value established by an NIH Consensus Development Conference Statement issued in 1991. This cut-point value is commonly used in obesity studies. CMS is receptive to reviewing new evidentiary criteria that may further define its coverage determinations. CMS strongly prefers data to be published or accepted for publication in a peer reviewed journal to be utilized in formulating an NCD.

Comments without Evidence

Comment: The commenters who submitted a standardized letter additionally made the following point: CMS should consider using its coverage with evidence development (CED) process as a means of covering surgery of type 2 diabetics with a BMI < 35, perhaps by using the data collection services of existing Bariatric Surgery Centers of Excellence and/or the Surgical Review Corporation’s Bariatric Outcomes Longitudinal Database (BOLD™). Also, two parties suggested that CMS simply defer making a coverage determination on surgery for persons of lesser BMI pending receipt of additional evidence.

Response: CMS believes that the evidence does not warrant a CED decision for diabetes surgery with persons having a BMI < 35. Further, we believe that a final decision should be made at this time, as required by §1862(l).

Comment: Some parties raised the issue of specification of the role of preoperative weight loss or prior medical treatment for weight loss as a prerequisite for surgery among persons with a BMI ≥ 35. Some thought that no prerequisites should exist, as they may be used or perceived as barriers to care, while others expressed the view that prerequisites should exist, similar to those in NCD 100.1, such that the beneficiary must have been previously unsuccessful with medical treatment for obesity and/or diabetes in order to obtain surgery. It was further suggested that Medicare should provide coverage for medical weight loss management for those Medicare patients that may benefit from it prior to undergoing bariatric surgery.

Response: The "Surgery for Diabetes" coverage determination maintains the sameopinion with respect to the medical treatment for weight loss as is contained in the Analysis section of NCD 100.1 (i.e., that medical treatment for weight loss should be "shown to be unsuccessful before considering a patient for bariatric surgery" and that although "*There are no consistent standards in the literature regarding length of a medical treatment trial and, therefore, we are unable to specify a specific time interval*. *A number of trials and guidelines recommend 6 to 12 months and we believe that to be reasonable." Coverage of medical weight loss management is not an element of this coverage determination.*

Comment: Additional specific concerns regarding coverage of surgery among Medicare beneficiaries with type 2 diabetes and a BMI $\geq$ 35 centered around the need for additional research involving studies of: which specific types of surgery may provide the greatest benefit; the pathophysiology underlying the impact of various types of gastric bypass and other similar surgeries on diabetes; longer-term (3-5 year) controlled trials involving larger patient cohorts to investigate fully the balance of net harms and benefits of surgery; the generalizability of results to the Medicare population; comparisons of surgery to standard therapy for diabetes so that decisions regarding surgery do not rely simply on case series without a contemporaneous true control group; which patient populations might benefit most from surgery, including the level of severity or stage of type 2 diabetes of the patient; and, decision analytic modeling of the effects of surgery on Hemoglobin A1C.

Response: CMS agrees that additional research is needed in these areas.

Comment: It was suggested that CMS further specify that beneficiaries with type 2 diabetes and a BMI $\geq$ 35 be eligible for surgical coverage without requiring that type 2 diabetes be treated with insulin or that the beneficiary have a history of being poorly controlled or refractory to medical therapy, based upon evidence showing that bariatric surgical procedures improve glycemic control not only in patients diagnosed with type 2 diabetes, but also in patients with impaired glucose tolerance.

Response: CMS is not requiring treatment-related characteristics of diabetes as part of this decision.

Comment: A number of providers and lay persons provided anecdotal comments regarding the benefits of surgery among persons of lesser BMI.

Response: CMS gives little weight to anecdotes in making its coverage determinations, generally preferring to evaluate the evidence contained in published, peer-reviewed scientific articles.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act §1862(l)(6)(A). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." §1862(a)(1)(A) of the Act.

Medical treatment for diabetes in obesity includes dietary manipulation, behavior modification and medication. These therapies have been tried individually and in combination, but with only limited long-term success. However, based on the lower risk-benefit ratio for medical treatment, we believe it should be routinely attempted and shown to be unsuccessful before considering a patient for surgery. There are no consistent standards in the literature regarding length of a medical treatment trial and, therefore, we are unable to specify a time interval. A number of trials and guidelines recommend six to 12 months and we believe that to be reasonable.

Since we found no direct comparative trials of surgery to specific medication or dietary regimens, we examined trials of medications and/or diet for some perspective. Tuomilehto et al., (2001) in a Swedish RCT of 522 persons all with IGT and mean age 55, average BMI 31, one placebo group and one treated with lifestyle interventions (diet, counseling), measured incidence of T2DM and found that, over four years, the incidence T2DM was 23% in the control group and 11% in the intervention group, a statistically significant difference. Fujioka et al., (2000) performed a double blind RCT comparing pharmacological treatment plus diet to diet plus placebo in 89 persons (treatment with Sibutramine) vs 86 persons (placebo) over 24 weeks. Treatment was associated with small mean decreases in blood glucose in sibutramine-treated patients who lost $\geq$ 5% of their weight, but it was not statistically significantly different from controls until the 10% weight loss group was tested. Sibutramine produced statistically and clinically significant weight loss when used in combination with recommendations for moderate caloric restriction. This weight loss was associated with improvements in metabolic control and quality of life, and sibutramine was generally well tolerated in obese patients with type 2 diabetes. HbA1C was stable in the control group and had a significant drop of 1.65 in the sibutramine group who lost 10% of their body weight over 24 weeks. We note that this does not match the success with bariatric surgery, and though the study included persons with BMI $\geq$ 27, the mean BMI was 34 in both groups.

CMS also notes that there are no long term data of import that support maintenance of weight loss using pharmacologic agents and it is not practical to assume that any but a small portion of patients will maintain weight loss as compared to post bariatric surgery.

In this decision we were focused on the question: Is the evidence sufficient to conclude that the following bariatric surgery procedures will improve health outcomes for Medicare patients with diabetes:

a. Roux-en-Y gastric bypass;
b. Laparoscopic adjustable gastric banding;
c. Biliopancreatic diversion with duodenal switch; or
d. Sleeve gastrectomy?

Medicare currently covers specific bariatric surgical procedures in certified centers for persons with BMI $\geq$ 35 and at least one comorbidity related to obesity (NCD Manual Section 100.1). We do not specify those comorbidities in that NCD.

BMI < 35

Studies of patients with BMI less than 35 included 3 randomized controlled trials, all involving LAGB. Studies of the other procedures were limited to clinical case series, which generally have small sample size and lack a comparison group, which limits our ability to draw conclusions about causality.

In all, we have outcomes data for bariatric surgery operations in 200 or so patients with diabetes and BMI's ≤35. Of that group, very few were over the age of 65 years. The nine studies involved patients in different countries, in a wide variety of study types, with varied surgical types, varied duration of diabetes and with little data on many risk factors. The one RCT, while showing benefit of surgery in mildly obese patients, also showed significant improvements with medical therapy. It did not provide a comparison of adverse events. The observational studies were, in general, small in numbers, lacked older patients and were unable to determine the benefit over medical management.

BMI ≥ 35

Studies of patients with BMI ≥ 35 were quite extensive and included a meta-analysis, two review articles, randomized controlled clinical trials [Swedish SOS Study (Sjostrom et al. 2000, 2004, 2007) Dixon's Australian study (2008), Lee's Taiwan study (2005)] and numerous cohort studies.

Of the papers that focus on many forms of bariatric surgery, the meta-analysis by Buchwald et al. in JAMA (2004) is one of the most prominent because it is systematic and draws data from 134 studies from around the world in its listing of results and drawing of conclusions. Therefore, we pay particular attention to it in our analysis. As we noted above in the evidence section, within those 134 studies were 179 treatment groups and 22,094 patients either enrolled or analyzable in the data set, including those in comparator control groups. Included were 5 randomized controlled trials, 28 nonrandomized controlled trials or series with comparison groups, and 101 uncontrolled case series. There was a difference in diabetes outcomes in all operative procedures. The positive effect of bariatric surgery on resolution of T2DM was highest in BPD (98.9%), next highest in GBP (83.7%), third highest in gastroplasty (71.6%) and fourth highest in gastric banding (47.9%).

There were a small number of RCTs and numerous observational studies that all demonstrated improvement in diabetes and glucose abnormalities following bariatric surgery. Complete resolution of glucose abnormalities ranged from approximately 50% to 100% in the articles. Evidence from RCTs for this NCD comes from the Swedish SOS Study (Sjostrom et al. 2000, 2004, 2007) and Dixon's Australian study (2008). Their studies demonstrated that bariatric surgery appears to be a viable option for the treatment of severe obesity, resulting in long-term weight loss, improved lifestyle and amelioration of the risk factor of diabetes and its incidence as well as decreased overall mortality. They also show that a maintained weight reduction of 16% strongly counteracted the development of diabetes over eight years.

In other cohort studies reviewed there was impressive surgical success with regards to resolution of T2DM which persisted over the long term, as much as 10-20 years. The successful surgical types aiding T2DM resolution and that CMS believes are supported by the evidence are LAGB (Dixon 2002, Ponce 2004, Lee 2005, Wickremesekera 2005, Pontiroli 2002, Nugent 2008), RYGBP (Schauer 2000, 2003, Sugerman 2003, 2004, Torquati 2005, Vidal 2007, White 2005, Wittgrove 2000, Skroubis 2006 and Alexandrides 2007), and BPD (Marceau 1998, Scopinaro 2005, Marinari 2006, Larrad 2004, Valera-Mora 2005).

Two reviews by Greenway 2002 and Ferchak 2004 on the effect of bariatric surgery on T2DM included many citations. Greenway stated that mortality was between 0.5 and 1.5% and that DM is resolved in the vast majority of patients after bariatric surgery. Ferchak stated that resolution of T2DM after LAGB was between 50 and 60%, whereas after RYGBP it was between 80 and 90%. Evidence regarding improvement in survival in bariatric surgery patients was reported in Adams (2007), Christou (2004) and others in large cohort studies.

Health Disparities

As noted above, the prevalence of diabetes mellitus increases with age over 50 years and is higher in black individuals compared to white individuals. Since the data on outcomes following bariatric surgery in individuals with type 2 diabetes have not been consistently reported by age or race subgroups, this decision does not specifically address these subgroups.

Conclusion

CMS does not believe that the current evidence demonstrates improved health outcomes for diabetic Medicare patients undergoing bariatric surgery with a BMI < 35. Therefore, we have determined that bariatric surgery is not reasonable and necessary for Medicare beneficiaries with a BMI < 35 as a treatment for diabetes and we are issuing a noncoverage decision.

We would ideally like to see an adequately powered RCT (multi-center if possible) with a control arm of medical treatment, with the ability to evaluate outcomes in subgroups of BMI above and below 35. Furthermore, we desire the ability to draw conclusions about conventional bariatric surgery types such as RYGBP, LAGB, and BPD.

CMS currently provides coverage for certain bariatric surgery procedures for Medicare beneficiaries with a BMI ≥ 35 who have at least one comorbidity. We do not define or list those comorbidities. The data reviewed clearly indicate that diabetes is improved following bariatric surgery in the obese population with a BMI ≥ 35. Thus, this coverage determination finds that it is reasonable and necessary to list diabetes as a comorbidity in NCD 100.1 and we are modifying that NCD to reflect this decision.

IX. Decision

The Centers for Medicare & Medicaid Services (CMS) has determined the following:

1) The evidence is not adequate to conclude that open and laparoscopic Roux-en-Y gastric bypass (RYGBP), laparoscopic adjustable gastric banding (LAGB), and open and laparoscopic biliopancreatic diversion with duodenal switch (BPD/DS) improve health outcomes in Medicare beneficiaries who have type 2 diabetes mellitus (T2DM) and a body-mass index (BMI) <35. Therefore, these procedures are not reasonable and necessary for patients with type 2 diabetes and BMI < 35 under section 1862(a)(1)(A) of the Social Security Act.

2) The evidence is adequate to conclude that open and laparoscopic Roux-en-Y gastric bypass (RYGBP), laparoscopic adjustable gastric banding (LAGB), and open and laparoscopic biliopancreatic diversion with duodenal switch (BPD/DS) improve health outcomes in Medicare beneficiaries who have T2DM and a BMI ≥ 35. Type 2 diabetes mellitus is a comorbid condition related to obesity as defined in NCD Manual 100.1 (Bariatric Surgery for Treatment of Morbid Obesity).

This decision makes no changes to National Coverage Determination (NCD) Manual section 100.8 (Intestinal Bypass Surgery) and section 100.11 (Gastric Balloon for Treatment of Obesity). Treatments for obesity alone remain non-covered.

Appendix A: General Methodological Principles of Study Design

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine whether: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

CMS normally divides the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits.

The issues presented here represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has unique methodological aspects.

1. Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to help ensure adequate numbers of patients are enrolled to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias)
- Co-interventions or provision of care apart from the intervention under evaluation (confounding)
- Differential assessment of outcome (detection bias)
- Occurrence and reporting of patients who do not complete the study (attrition bias)

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies
- Retrospective case control studies
- Cross-sectional studies
- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series

- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study's selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess the evidence.

2. Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens, and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease, and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing, and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage decisions for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation), and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations because one of the goals of our determination process is to assess health outcomes. We are interested in the results of changed patient management not just altered management. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

3. Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Improved health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. For most determinations, CMS evaluates whether reported benefits translate into improved health outcomes. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

Appendix B – Proposed policies

100.1 - Bariatric Surgery for Treatment of Morbid Obesity

A. General

…

B. Nationally Covered Indications

Open and laparoscopic Roux-en-Y gastric bypass (RYGBP), open and laparoscopic Biliopancreatic Diversion with Duodenal Switch (BPD/DS), and laparoscopic adjustable gastric banding (LAGB) are covered for Medicare beneficiaries who have a body-mass index ≥ 35, have at least one co-morbidity related to obesity, and have been previously unsuccessful with medical treatment for obesity. These procedures are only covered when performed at facilities that are: (1) certified by the American College of Surgeons as a Level 1 Bariatric Surgery Center (program standards and requirements in effect on February 15, 2006); or (2) certified by the American Society for Bariatric Surgery as a Bariatric Surgery Center of Excellence (program standards and requirements in effect on February 15, 2006).

Type 2 diabetes is a co-morbidity for purposes of this NCD.

A list of approved facilities and their approval dates are listed and maintained on the CMS Coverage Web site at http://www.cms.hhs.gov/center/coverage.asp, and published in the Federal Register.

C. Nationally Non-covered Indications

The following bariatric surgery procedures are non-covered for all Medicare beneficiaries:

- Open adjustable gastric banding
- Open and laparoscopic sleeve gastrectomy; and
- Open and laparoscopic vertical banded gastroplasty.

D. Other

100.14 - Surgery for Diabetes **(new section)**

A. General

Medicare currently covers bariatric surgery for persons with diabetes and a BMI ≥ 35. Surgical procedures that are used in this context are discussed in section 100.1 of the NCD manual (above). It has been proposed that these same procedures may be beneficial for beneficiaries with type 2 diabetes who do not meet the criteria for treatment of morbid obesity. We specifically evaluated the evidence associated with surgery among persons with type 2 diabetes to assess the effectiveness of such procedures in reducing the signs and symptoms of this disease in Medicare beneficiaries with BMI < 35.

B. Nationally Covered Indications

See the NCD manual section 100.1.

C. Nationally Non-covered Indications

Open and laparoscopic Roux-en-Y gastric bypass (RYGBP), open and laparoscopic Biliopancreatic Diversion with Duodenal Switch (BPD/DS), and laparoscopic adjustable gastric banding (LAGB) are non-covered for Medicare beneficiaries with a BMI <35 and type 2 diabetes.

D. Other

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